ROBUST SUMMARY DATA SET

FOREWARD

Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

Memo:	Triisopropylborate (TIPB) dataset for HPV prepared by INVISTA S. à r. l.
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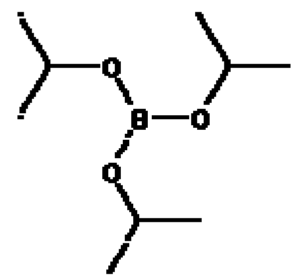
Chapter Profile	Chapter 1 - Substance Information: 1.0 Chapter 2 - Physical/Chemical Properties: 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, and 2.8. Chapter 3 - Environmental Fate: 3.1, 3.2, 3.3, 3.4, and 3.5. Chapter 4 - Ecotoxicity: 4.1, 4.2, and 4.3. Chapter 5 – Mammalian Toxicity: 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7 and 5.8

<u>**Triisopropylborate (TIPB) HPV Robust Summary**</u>

1. General Information **10 March 2007** **Substance ID: 5419-55-6**

1.0 Substance Information

Existing Chemical	Triisopropylborate
CAS Number:	5419-55-6
Chemical Name:	Boric acid (H_3BO_3), tris (1-methylethyl) ester
EINECS Name	Triisopropyl Borate
EC Number	226-529-9
Molecular Formula	$C_9H_{21}BO_3$
Structural Formula:	



Other Names:	Triisopropylborate (TIPB) Boric acid, triisopropyl ester Boric acid (H_3BO_3), triisopropyl ester Boron isopropoxide Boron triisopropoxide Isopropyl borate Triisopropoxyborane Triisopropoxyboron Triisopropyl orthoborate Boric Acid (H_3BO_3), Tris (1-Methylethyl) Ester
Exposure Limits:	No Data for Triisopropylborate

2.0 Physical/Chemical Properties

2.1 Melting Point

Value: -70 to -72 °C

Decomposition: No Data

Sublimation: No Data

Pressure: No Data

Method: No Data

GLP: Unknown

Reference: Invista (2004). Material Safety Data Sheet 130000018085 (May 1).

Reliability: Not assignable because limited study information was available.

Additional Reference for Melting Point:

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 10th ed., p. 2157, John Wiley & Sons, Inc., New York.

2.2 Boiling Point

Value: 140 °C

Decomposition: No Data

Pressure: 760 mm Hg

Method: No Data

GLP: Unknown

Reference: Lide, D. R. (ed.) (2001-2002). Handbook of Chemistry and Physics, 82nd ed., CRC Press, Boca Raton, FL.

Reliability: Not assignable because limited study information was available.

Additional References for Boiling Point:

Invista (2004). Material Safety Data Sheet 130000018085 (May 1).

Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 10th ed., p. 2157, John Wiley & Sons, Inc., New York.

2.3 Density

Value: 0.8251 g/cm^3

Temperature: 20 °C

Method: No Data

GLP: Unknown

Results: No additional data.

Reference: Lide, D. R. (ed.) (2001-2002). Handbook of Chemistry and Physics, 82nd ed., CRC Press, Boca Raton, FL.

Reliability: Not assignable because limited study information was available.

Additional Reference for Density:
Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 10th ed., p. 2157, John Wiley & Sons, Inc., New York.

2.4 Vapour Pressure

Value: 8.6 mm Hg

Temperature: 25 °C

Decomposition: No Data

Method: Measured

GLP: Unknown

Reference: Invista (2004). Material Safety Data Sheet 130000018085 (May 1).

Reliability: Not assignable because limited study information was available.

Additional References for Vapor Pressure: None Found.

2.5 Partition Coefficient

Partition Coefficient	Octanol - Water
Log Kow:	Triisopropylborate: 0.83 (estimated) Isopropanol (hydrolysis product) = 0.28 (estimated) Boric acid (hydrolysis product) = -0.22 (estimated)
Temperature:	25 ^{o}C
Method:	Modeled. KOWWIN, v.1.67, module of EPIWIN v.3.11 (Syracuse Research Corporation). KOWWIN uses "fragment constant" methodologies to predict log P. In a "fragment constant" method, a structure is divided into fragments (atom or larger functional groups) and coefficient values of each fragment or group are summed together to yield the log P estimate.
GLP:	Not Applicable
Reference:	Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.
Reliability:	Estimated value based on accepted model.

Additional References for Partition Coefficient (log Kow): None Found.

2.6 Solubility in Different Media (Water)

Value:	0% (unstable in water, hydrolyzes rapidly, <15 minutes)
Temperature:	25-37 ^{o}C
pH/pKa:	pH range = 1.2-9
Method:	OECD 111
GLP:	Yes
Reference:	SafePharm Laboratories, Inc., Triisopropylborate (TIPB): Determination of Hydrolysis as a Function of pH. SPL Project Number 2231/0013
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Water Solubility: See Section 3.2.

2.7 Flash Point

Value: 27.8 °C

Method: TCC

GLP: Unknown

Reference: Lewis, R. J., Sr. (2000). Sax's Dangerous Properties of Industrial Materials, 10th ed., p. 2157, John Wiley & Sons, Inc., New York.

Reliability: Not assignable because limited study information was available.

Additional References for Flash Point:

Invista (2004). Material Safety Data Sheet 130000018085 (May 1).

Lide, D. R. (ed.) (2001-2002). Handbook of Chemistry and Physics, 82nd ed., CRC Press, Boca Raton, FL.

2.8 Flammability

Results: Flammable liquid

Method: No Data

GLP: Unknown

Reference: Invista (2004). Material Safety Data Sheet 130000018085 (May 1).

Reliability: Not assignable because limited study information was available.

Additional References for Flammability: None Found.

3.0 Environmental Fate

3.1 Photodegradation

Concentration: No Data

Temperature: No Data

Direct Photolysis: The hydrolysis products, isopropanol and boric acid, are not expected to be subject to direct photolysis (Harris, 1990), due to a lack of significant absorbtivity above 290 nm.

Indirect Photolysis: Triisopropylborate has an estimated half-life due to OH radical oxidation of 10.55 hours.

Breakdown Products: No Data

Method: Direct Photolysis: Inspection of chemical structure.
Indirect Photolysis: Modeled

GLP: Not Applicable

Reference: AOPWIN, v1.91 module of EPIWIN v.3.11. Meylan, W. M. and P. H. Howard (1993). Chemosphere, 26:2293-99. The model used assumptions of a 24-hour day and an ambient hydroxyl radical concentration of 0.5×10^6 molecules/cm^3.
Harris, J. C. (1990). Rate of Aqueous Photolysis, Chapter 8, In: Handbook of Chemical Property Estimation Methods, Lyman, W. J. et al. (eds.), American Chemical Society, Washington, DC.

Reliability: Estimate based on known qualitative structure-activity relationships.

Additional References for Photodegradation: None Found.

3.2 Stability in Water

Concentration: No Data

Half-life: Significantly less than 15-minutes at pH 9
Significantly less than 15-minutes at pH 7
Significantly less than 15-minutes at pH 4
Significantly less than 15-minutes at the physiologically important pH of 1.2.

% Hydrolyzed: Complete (100%)

Method: The study protocol was similar to OECD Guideline 111 (Hydrolysis as a Function of pH). 0.2206g of Triisopropylborate (TIPB) was dissolved in 50 mL of prepared deuterated chloroform. The chloroform had a tetramethylsilane (TMS) internal standard and prior to the addition of TIPB; the chloroform solution had been dried with anhydrous sodium sulfate and filtered.

An aliquot of the TIPB in deuterated chloroform was transferred to a clean, dry NMR tube and stored under nitrogen. The remaining TIPB in deuterated chloroform was transferred in 10 mL aliquots to four, capped glass vessels.

The pH 9 buffer (0.01 M disodium tetraborate with 0.02 M sodium chloride) solution, pH 7 buffer was prepared by filtering through a 0.2 µm filter, sonicated to degas, and purged with nitrogen to prevent degradation. 10mL of the buffer was added to one of the capped, glass vessels containing the TIPB in deuterated chloroform. The capped glass vessel was shaken and placed in a water bath for 15 minutes and protected from exposure to light. The temperature of the water bath was not specified. Then, visible aqueous phases were removed and the solution that remained was dried with anhydrous sodium sulfate. An aliquot was transferred to a clean, dry NMR tube and stored under nitrogen.

The following sample blanks were prepared: The deuterated chloroform solution prepared as detailed for the TIPB sample was added to a capped, glass vessel. Buffer solution prepared as detailed was added to the capped, glass vessel. The buffered solution in the glass vessel was similarly treated and handled as detailed for the buffered TIPB sample. A sample containing isopropanol (propan-2-ol) was also similarly prepared as a reference solution for the anticipated hydrolysis product. No boric acid reference solution was prepared as it would not be detected by ^{1}H Nuclear Magnetic Resonance.

The samples were analyzed using Bruker DPX 300 Nuclear Magnetic Resonance (NMR) system at ambient temperature and frequency of 300 MHz. NMR spectra for the TIPB in deuterated chloroform, the buffered TIPB in deuterated chloroform, isopropanol, and buffer sample blank solutions were generated and compared.

Results: For the TIPB in deuterated chloroform solution with TMS internal standard, the methane protons for the borate ester were detected at approximately 4.3 to 4.6 ppm. Isopropanol was also detected at approximately 4.0 ppm and highlights the hydrolytic instability of the parent compound.

For the four buffered TIPB solutions, no parent compound remained and isopropanol was detected at approximately 4.0

ppm. Analysis of the isopropanol reference solution confirmed the hydrolysis product in the buffered TIPB solutions and the TIPB in the deuterated chloroform was isopropanol. Isopropanol was not present in the buffered solution sample blanks and deuterated chloroform sample blank.

Some of the parent compound could have partitioned into the aqueous phase. Based on the estimated log Kow of 8.3, it was concluded, that most, if not all of the test material would have remained in the organic phase. The loss of the parent compound in the buffered test solutions was attributed to hydrolysis.

GLP: Yes.

Reference: SafePharm Laboratories, Inc., Triisopropylborate (TIPB): Determination of Hydrolysis as a Function of pH. SPL Project Number 2231/0013

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Stability in Water: None Found.

3.3 Transport Between Environmental Compartments (Fugacity)

Media: Air, Water, Soil, and Sediment

Distributions:

Compartment	% of total distribution	½ life (hours) (advection + reaction)
Air	7.93	10.5
Water	61.5	360*
Soil	30.5	720
Sediment	0.12	3240

* ½ life will be lowered by hydrolysis, which is not treated by this model

Adsorption Coefficient: K_{oc} = 2.77

Desorption: No Data

Volatility: Henry's Law Constant = 0.000647 atm-m^3/mole

Method: Modeled assuming equal emission to air, water, and soil of triisopropylborate (CAS Registry # 5419-55-6).

Henry's Law Constant: 0.000647 atm-m^3/mole (calc VP/Wsol)

Vapor Pressure: 100 mm Hg (user-entered)

Log Kow: 0.83 (KOWWIN program)

Soil K_{oc}: 2.77 (calc by model)

Henry's Law Constant - HENRYWIN v.3.10 module of EPIWIN v.3.11 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

K_{oc} – Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v.3.11 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v.3.11 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments.

GLP: Not Applicable

Reference: HENRYWIN -

J. Hine and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v.3.11 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated values based on accepted models.

Additional References for Transport (Fugacity): None Found.

3.4 Biodegradation

No data for triisopropylborate exists, since the chemical rapidly hydrolyzes to boric acid and isopropanol. Therefore, for this robust summary, supporting data for the hydrolysis products are presented.

Data for Hydrolysis Product: Isopropanol

Value:	The hydrolysis product, isopropanol, is readily biodegradable and averaged 86% of ThBOD.
Breakdown Products:	No Data
Method:	MITI 14-day test (OECD Guideline 301C). The inoculum contained 30 mg/L of activated sludge.
GLP:	Yes
Reference:	Chemicals Evaluation and Research Institute, Japan http://qsar.cerij.or.jp/cgi-bin/QSAR/index.cgi?e
Reliability:	High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric Acid

Value:	The hydrolysis product, boric acid, is not subject to biodegradation.
Breakdown Products:	Not Applicable
Method:	Not Applicable
GLP:	Not Applicable
Reference:	Not Applicable
Reliability:	Not Applicable

Additional References for Biodegradation: None Found.

3.5 Bioconcentration

Value: BCF – Isopropylborate (parent): 0.5 (estimated)
BCF - Isopropanol (hydrolysis product): 0.5 (estimated)
BCF – Boric acid (hydrolysis product): 0.5 (estimated)

Method: Modeled. BCFWIN v. 2.15 module of EPINWIN v.3.11 (Syracuse Research Corporation). BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (Kow) with correction factors based on molecular fragments.

GLP: Not Applicable

Reference: "Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient",

SRC TR-97-006 (2nd Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC, Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil Gouchie, Syracuse Research Corp.

Reliability: Estimated values based on accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute/Prolonged Toxicity to Fish

No data for triisopropylborate exists, since the chemical rapidly hydrolyzes to boric acid and isopropanol. Therefore, for this robust summary, supporting data for the hydrolysis products are presented.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: **96-hour LC_{50}**

Species: *Pimephales promelas*, fathead minnow

Value: 9,640-10,400 mg/L

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The 96-hour LC_{50} was determined with Environmental Research Laboratory-Duluth cultured fathead minnows using a flow-through proportional diluter and a modified Benoit continuous-flow minidiluter system. Lake Superior water maintained at 25±1°C was used in the test, and data were recorded for hardness, total alkalinity, pH, and dissolved oxygen.

Twenty to 25, 30-day-old fish, each weighing approximately 0.12 g were randomly divided among the test tanks (control and 5 different concentrations in duplicate). Fish were not fed during the test. Deaths were recorded after 1, 3, 6, 12, 24, 48, 72, and 96 hours, and the median lethal concentration (LC_{50}) was computed using the trimmed Spearman-Karber method. Additional details, including concentrations tested, number of fish per concentration, and loading rate, were not reported.

Concentrations of test chemical in water were measured daily at each exposure level. Water was analyzed by gas chromatography or UV spectroscopy and spectrofluorimetry.

GLP: No

Test Substance: Isopropanol, purity not reported

Results: Routine measures of hardness and total alkalinity of test water yielded mean values of 45.5 and 42.2 mg/L as $CaCO_3$, respectively. The mean of the pH was 7.5, and dissolved oxygen was always greater than 60% of saturation. Additional data, including mortality and effect per concentration and control response, were not reported.

Reference: Veith, G. D. et al. (1983). Can. J. Fish. Aquatic. Sci., 40:743-748.

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric acid (10043-35-3)

Type: **96-hour LC_{50}**

Species: *Oncorhynchus tshawytscha*, Chinook salmon
Oncorhynchus kisutch, Coho salmon

Value: 725 mg/L (95% confidence interval, 590-890 mg/L; Chinook salmon; freshwater)

600 mg/L (95% confidence interval, 511-706 mg/L; Chinook salmon; brackish water)

447 mg/L (95% confidence interval, 356-561 mg/L; Coho salmon; fresh water)

600 mg/L (95% confidence interval, 511-705 mg/L; Coho salmon; brackish water)

Method: Static acute toxicity tests were conducted according to procedures recommended by ASTM (Report E-729).

Fish were fed a commercial salmon diet. Tests were conducted in 3 reconstituted waters. The characteristics of 2 of the dilution waters were designated to simulate water qualities for major anions and cations in which standardized San Luis Drain water without trace elements, was diluted 10-fold in a standardized fresh receiving water or 22.5-fold in a standardized brackish receiving water. The 3rd water was standard soft water prepared as recommended by the U.S. EPA for use in acute toxicity tests with fish.

The various water types were reconstituted in reverse osmosis-deionized water by varying the type and quantity of mineral salts added. Water quality characteristics were measured according to methods recommended by the APHA and U.S. EPA. For each type of dilution water, there was only a small amount of variation among batches prepared, as evidenced by the low coefficient of variation (<5%) for each measured characteristic. Dilution water characteristics are included in the table below.

Water Type:	Fresh	Brackish	Soft
Conductivity (µmhos/cm @ 25°C)	721	2887	157

pH	7.82	7.79	7.57
Hardness (mg $CaCO_3$/L)	211	333	41.7
Calcium (mg/L)	45.8	37.4	7
Magnesium (mg/L)	23.6	58.4	6
Sodium (mg/L)	73	469	13
Alkalinity (mg $CaCO_3$/L)	87.2	36.6	29.6
Chloride (mg/L)	59.2	726	<1
Sulfate (mg/L)	185.9	291	47

Test solutions were prepared in deionized water on the day of use or by adding the test substance directly to the test vessel. Nominal concentrations reported were expressed as the total element added as determined from the certificate of analysis for the test substance.

Static 96-hour exposures were conducted in 19.6-L glass jars containing 15 L of test solution and maintained at 12±1°C in temperature-controlled water baths. Each test consisted of exposing groups of 10 fish to a series of toxicant concentrations that differed by 60% between treatments, and a control. Concentrations tested and number of fish per concentration were not reported.

For large, advanced fry, duplicate sets of jars were used and only 5 fish were stocked in each jar to maintain loading densities of 0.8 g/L or lower. Observations of mortality and abnormal behavioral responses were made at 24-hour intervals, and all dead fish were removed after each observation.

In one (1) set of tests, 2 life stages of Chinook salmon and Coho salmon were tested with boric acid. One life stage composed of swim-up fry 8-12 weeks old (post hatch) tested in fresh water. The 2nd life stage composed of advanced fry 15-21 weeks old tested in brackish water. Chinook salmon were also tested in soft water.

In tests conducted in the 2 site-specific waters, pH was measured at the beginning and end of the test.

Eyed eggs, alevins, and swim-up fry of Chinook salmon were tested in soft water to determine the relative sensitivity of those various life stages to boron. Tests with eyed eggs and alevins were conducted in the dark in glass jars containing test solution. Due to their rapid development, these life stages were acclimated for only 24 hours before testing. Swim-up fry were tested in solution under natural laboratory lighting. Groups of 25 eggs, 10 alevins, or 10 swim-up fry were exposed to a series of toxicant concentrations that differed by 56% between treatments, and a control. Concentrations tested and number of fish per concentration were not reported.

Criteria of death for eggs were the presence of an opaque (whitened) membrane. Alevins were examined under 30x magnification for the absence of a heartbeat, which was the criterion for death.

The method of Litchfield and Wilcoxon was used to calculate LC_{50} values. The Standard Error of the Difference was used to determine statistical differences in LC_{50} values.

GLP: No

Test Substance: Boric acid, actual purity not reported (test substance reported as "reagent grade or highest grade available from supplier")

Results: The 24-hour LC_{50} of Chinook and Coho salmon (fresh or brackish water) was >1000 mg/L. Boron was relatively non-toxic. Young Coho salmon tested in fresh water were less tolerant than older fish tested in brackish water and Chinook salmon tested in either dilution water. The relative sensitivity of various early life stages of Chinook salmon to boron changed significantly as the fish developed. Fry were consistently more sensitive than either the embryos or alevins to boron. No additional details, including mortality and effects per concentration were reported.

The pH in test concentrations and controls were not markedly different, ranging from 6.5 to 8.1. No significant differences in 96-hour LC_{50} values were found among dilution water qualities, thus indicating that differences in water quality characteristics tested did not modify the toxicity of these chemicals.

Reference: Hamilton, S. J. and K. J. Buhl (1990). Arch. Environ. Contam. Toxicol., 19:366-373.

Reliability: Medium because a suboptimal study design (nominal test concentrations) was used.

Data for Hydrolysis Product: Boric acid (10043-35-3)

Type: **96-hour LC_{50}**

Species: *Ptychocheilus lucius*, Colorado squawfish
Xyrauchen texanus, Razorback sucker
Gila elegans, Bonytail

Value: 279 mg/L, as boron (Colorado squawfish; swim-up fry 17-31 day)

>100 mg/L, as boron (Colorado squawfish; juvenile 99-115 day)

527 mg/L, as boron (Colorado squawfish; juvenile 193-207 day)

233 mg/L, as boron (Razorback sucker; swim-up fry 10-17 day)

279 mg/L, as boron (Razorback sucker; juvenile 133-139 day)

>100 mg/L, as boron (Razorback sucker; juvenile 176-178 day)

280 mg/L, as boron (Bonytail; swim-up fry 11-18 day)

>100 mg/L, as boron (Bonytail; juvenile 138-145 day)

553 mg/L, as boron (Bonytail; juvenile 220-234 day)

Method: Static acute toxicity test procedures closely followed those outlined by the American Society for Testing and Materials (ASTM) (1989).

Fish were fed a commercial diet supplemented for the first 30 days with live nauplii of brine shrimp. The water quality for egg and larval culture was pH 7.7-7.9, hardness 233-330 mg/L, and alkalinity 174-226 mg/L. All tests were conducted in a reconstituted water quality designed to simulate site-specific conditions for major cations and anions, without trace elements, in the Green river. Reconstituted water was prepared and water quality characteristics were measured for each tank of dilution water.

Test solutions of boric acid were prepared as a stock solution or by adding the test substance directly to the test vessel. Stock solutions were formulated in deionized water on the day of use. Nominal concentrations reported were expressed as the total inorganic toxicant added, as determined from the certificate of analysis for the test substance.

Each test consisted of exposing groups of 10 fish to a geometric series of 6-8 nominal concentrations (concentrations not reported) and a control for 96 hours. Tests with fry were conducted in 3.8 L-glass jars filled with 3 L of test solution and those with juveniles in 19.6-L glass jars filled with 15 L of test solution. For larger juveniles (1.2 g), duplicate sets of jars were used, and only 5 fish were placed in each jar to maintain loading densities of 0.8 mg/L or less. Temperature was maintained at 25±1 °C by immersing the jars in temperature-controlled water baths. Because of their rapid rate of development, fry were acclimated to the dilution water for only 24 hours before testing. Juveniles were acclimated simultaneously to the dilution water and test temperature over a 2-day period and were held in the dilution water for 2 days prior to testing. The fish were not fed during acclimation or testing.

At the start of each test, fish were randomly distributed to the test vessels within 30 minutes after the addition of the toxicant. To minimize handling stress, fry were first transferred to 50-mL beakers, containing a small volume of dilution water. After 10 fish were placed in a beaker, most of the water was decanted and the fish were gently poured into the jars. Juveniles were carefully netted from the holding tank and distributed in groups of 2 to each jar. Mortality was recorded, and all dead fish were removed at 24-hour intervals. Fry without perceivable movement of the pectoral fins were pipetted from the jar and examined under 30x magnification for the absence of a heartbeat, which was the criterion for death. Total length and weight of the control fish were measured at the end of the tests.

Dissolved oxygen and pH were measured at the beginning and end of the tests in the control, low, medium, and high treatments with live fish present. Water quality characteristics included:

Conductivity (µmhos/cm @ 25°C)	610
Hardness (mg $CaCO_3$/L)	196
Calcium (mg/L)	46
Magnesium (mg/L)	20
Sodium (mg/L)	49
Alkalinity (mg $CaCO_3$/L)	107
Chloride (mg/L)	20
Sulfate (mg/L)	164

The LC_{50} values were calculated by the binomial method or the moving average-angle method, depending on the number of partial kills in a test, using a computer program. In tests with boron where less than half the fish died in the highest test concentration, the LC_{50} was reported as being greater than that concentration. For tests in which no partial mortalities occurred, the confidence intervals were given as follows: the upper limit was the lowest test concentration with 100% mortality, and the lower limit was the lowest test concentration with 0% mortality. All LC_{50} values were expressed as nominal concentrations of the inorganic toxicant, not the inorganic compound. The standard error of the difference was used to determine statistical differences in LC_{50} values.

GLP: No

Test Substance: Boric acid, purity not reported

Results: There was no significant difference among the 3 species in their sensitivity to the test substance. In general, the swim-up life stage was more sensitive to boron than the 2 older life stages of the 3 species. There was no mortality in the control treatments from the tests. No additional data, including mortality and effects per concentrations were reported.

Dissolved oxygen concentrations were maintained at or greater than 40% saturation in most tests; however, fish in control and low treatment tests with <40% saturation displayed no signs of stress. The pH of the test solutions ranged from 7.0 to 8.5 at 96 hours of exposure.

Reference: Hamilton, S. J. (1995). Ecotoxicol. Environ. Safety, 30:134-142.

Reliability: Medium because a suboptimal study design (nominal test concentrations) was used.

Data for Hydrolysis Product: Boric acid (10043-35-3)

Type: LC_{50}

Species: *Salmo gairdneri*, rainbow trout
Ictalurus punctatus, channel catfish
Carassius auratus, goldfish

Value: 150 ppm (95% confidence interval, 90-249 ppm; rainbow trout; at hatching; soft water)

100 ppm (95% confidence interval, 70-142 ppm; rainbow trout; 4 day post-hatching; soft water)

100 ppm (95% confidence interval, 61-163 ppm; rainbow trout; at

hatching; hard water)

79 ppm (95% confidence interval, 35-165 ppm; rainbow trout; 4 days post-hatching; hard water)

220 ppm (95% confidence interval, 167-290 ppm; channel catfish; at hatching; soft water)

155 ppm (95% confidence interval, 111-217 ppm; channel catfish; 4 day post-hatching; soft water)

102 ppm (95% confidence interval, 23-180 ppm; channel catfish; at hatching; hard water)

22 ppm (95% confidence interval, 19-25 ppm; channel catfish; 4 days post-hatching; hard water)

178 ppm (95% confidence interval, 131-242 ppm; goldfish; at hatching; soft water)

46 ppm (95% confidence interval, 32-66 ppm; goldfish; 4 day post-hatching; soft water)

170 ppm (95% confidence interval, 115-251 ppm; goldfish; at hatching; hard water)

75 ppm (95% confidence interval, 50-112 ppm; goldfish; 4 days post-hatching; hard water)

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Test animals were exposed to 10-14 concentrations of boric acid. Depending on the sensitivity of the species, tests were initiated at 50-300 ppm boron, and continued at 2- to 10-fold dilutions until LC_1 and LC_{50} values were determined.

Trout were exposed to 0.001, 0.01, 0.1, 0.5, 1, 5, 10, 25, 50, 100, or 200 ppm boric acid.

Catfish were exposed to 0.01, 0.05, 0.1, 0.5, 0.75, 1, 2.5, 5, 7.5, 10, 25, 50, 75, 100, 150, 200, or 300 ppm boric acid.

Goldfish were exposed to 0.05, 0.1, 0.5, 1, 5, 7.5, 10, 25, 50, 100, 200, or 300 ppm boric acid.

In all cases, exposure levels of boric acid were based on actual boron content (boron equivalents), and verified by the chemical analysis of culture water.

Boron treatment was initiated subsequent to fertilization and maintained continuously through 4 days post-hatching, giving exposure periods in days of 28, 9, and 7 for trout, catfish, and goldfish. Minimum sample size per test concentration was 125 for fish embryos (actual number per concentration was not reported). In the analyses of test results, embryos were classified as lethals, teratogenic (anomalous) survivors, or normal survivors.

Hatchability was based on all embryos that lived to complete the hatching process. Normal survivors were defined as animals free of the debilitating morphological defects that characterized teratogenic survivors. Test responses were expressed as frequencies in experimental populations/frequencies in controls.

Log probit analysis was used to statistically determine the LC_1 and LC_{50} values. The probit regressions were performed with an IBM computer, and were determined in each instance by using animal responses for the full range of test concentrations. When severely truncated survival curves precluded use of the computer program for LC_{50} determinations, the Litchfield-Wilcoxon graphic method was used. Analysis of variance and the t-test were used to determine statistical significance of differences in toxicity, water hardness levels, and other test variables.

The synthetic culture medium used for the boron bioassays was prepared from distilled, double deionized water, having a conductivity of 0.25 µmhos or less. Routing monitoring was conducted for background contaminants. The basic stock was prepared to give a water hardness level of 50 or 200 ppm (as $CaCO_3$) and a pH of 7.5-8.0. Different levels of hardness were achieved by dilution of the basic culture water. Chemical characteristics of synthetic culture water included:

Conductivity (µmhos/cm @ 25°C)	300
Hardness (mg $CaCO_3$/L)	200
Calcium (mg/L)	54.2
Magnesium (mg/L)	14.8
Sodium (mg/L)	27.4
Alkalinity (mg $CaCO_3$/L)	82
Chloride (mg/L)	98.2
Sulfate (mg/L)	58.5
Osmolarity (mOsm/kg H_2O)	12
Potassium (mg/L)	2.6
Bicarbonate (mg/L)	72.6

Boron bioassays were conducted using a continuous flow system. Fish eggs were cultured through 4 days post-hatching in glass chambers, through which test water was perfused at prescribed flow rates. The test substance was administered to a mixing chamber situated ahead of each culture dish, using graduated flow from a syringe pump. Synthetic water was delivered to the mixing chamber by regulated flow from a peristaltic pump. Flow rates from both syringe and peristaltic pumps were monitored by liquid flow meters.

The concentration of test substance delivered to the mixing chamber was regulated by adjusting the mixing ratio from the pumping units and/or by varying the concentration of test substance delivered from the syringe pump. Solutions from the 2 channels were mixed with a magnetic stirring bar, and delivered to the culture chamber under positive pressure. For test concentrations of 10 ppm or more, the boron compound generally was added directly to the culture water in the peristaltic pump reservoir, eliminating the need for the syringe pump channel. In such instances, the test substance remained stable at selected test concentrations for 24-hours or more in polyethylene containers, and important test parameters of culture water were not altered upon standing (e.g., pH, hardness).

The aquatic bioassay cultures were maintained in walk-in environmental rooms. Culture water was given continuous aeration in the peristaltic pump reservoirs. For the bioassays, pH ranged from 7.5-7.9. All cultures were monitored at regular daily intervals for temperature, dissolved oxygen, ammonia, water hardness, and pH. Flow rates from peristaltic and syringe pumps were monitored twice daily.

Boron exposure levels were determined at regular daily intervals by analysis of culture water. Test organisms were examined daily to gauge extent and frequency of development, and to remove dead specimens. Control eggs were also cultured.

Particular attention was given to trout embryos, especially during the "green stage." Harmful exposure to artificial light was precluded and cultures were maintained under semi-sterile conditions to minimize occurrences of soft egg disease and fungus. Prior to each use, culture rooms were disinfected and irradiated with UV for 12 hours, and the rooms were maintained under positive pressure. In bioassays with boron toxicant, a flow rate of 200 mL/hour, giving a turnover time of 1.5 hours, was maintained.

Trout eggs and sperm were collected for test purposes by artificial spawning and milking, using methods of Leitritz, 1972. Fertilization was accomplished by mixing sperm and eggs for 15 minutes immediately prior to the onset of boron exposure. For all other aquatic species, fertilized eggs were collected from natural spawn. Boron treatment was initiated up to 2 hours post-spawning for goldfish and catfish.

Quantitative determinations of boron were accomplished using the curcumin method. This technique proved applicable for a concentration range of 0.1-1.0 mg/L. Concentration and dilution of sample water were used to extend the analytical range. All lots of prepared culture water were monitored for possible boron contamination prior to use for bioassay purposes. To avoid possible contamination from borosilicate glassware, Vycor® brand evaporating dishes were used for analytical purposes.

GLP: No

Test Substance: Boric acid, actual purity not reported (test substance reported as "ACS grade")

Results: The concentration of ammonia was held below 0.1 ppm in all instances.

The temperature was 24.7-25.0, 24.8, and 13.3-13.7 °C for catfish, goldfish, and trout, respectively.

Dissolved oxygen was 7.3-7.6, 7.4-7.5, and 9.2-9.6 ppm for catfish, goldfish, and trout, respectively.

The pH was 7.5-7.6, 7.6-7.9, and 7.7-7.9 for catfish, goldfish, and trout, respectively.

Water hardness was 51.8, 54.4, and 54.1 ppm $CaCO_3$ at the 50 ppm test concentration in catfish, goldfish, and trout, respectively.

Water hardness was 212.0, 207.5, and 204.0 at 200 ppm $CaCO_3$ at the 200 ppm test concentration in catfish, goldfish, and trout, respectively.

In no instance was background boron contamination detected in the prepared culture water, including that used for the maintenance of control animals. Actual exposure levels <0.1 ppm were not reported, as analysis of standards prepared at 0.05 ppm or less were not fully reproducible. However, in all such cases, boron levels delivered by syringe pumps to mixing chambers were well above the detection limit, and direct analyses were conducted to confirm syringe pump boron concentrations. In addition, flow rates from syringe pumps (boron) and peristaltic pumps (culture water) were monitored at regular intervals, using both flow meters and direct volumetric measurements, to determine actual boron dilution ratios obtained in the mixing chambers. Dividing actual syringe pump boron concentrations by boron dilution ratios, final boron levels delivered to the bioassay test chambers usually were found to be within 3%, and always within 5%, of selected nominal exposure values. This alternative monitoring procedure was shown for trout bioassays, which included boron exposure values of 0.01 ppm (10 µg/L) and 0.001 ppm (1 µg/L). Though such measurements may be used to confirm boron concentrations delivered to test chambers, they do not provide direct measurements on the stability of exposure levels maintained within the bioassay cultures. While it is unlikely that actual boron exposure values could have exceeded the upper limit of variation (5%) shown for water supplied to the cultures, possible losses of boron from culture water, through tissue accumulation or other means, could have resulted in undetectable reductions in exposure concentrations. However, a high degree of culture stability was obtained for boron concentrations as low as 0.1 ppm, as determined by direct analyses of culture water.

Measured concentrations for tests in hard and soft water for trout, catfish, and goldfish are provided in the tables below.

Rainbow trout		
Nominal boron concentration boron (ppm)	Measured boron concentration (ppm) – soft water (50 ppm $CaCO_3$)	Measured boron concentration (ppm) – hard water (200 ppm $CaCO_3$)
0.001	Not reported	Not reported
0.01	Not reported	Not reported
0.1	0.11	0.10
0.5	Not tested	0.47
1	1.00	0.98
5	4.74	4.85
10	9.26	9.40
25	23.50	23.80
50	45.50	48.30
100	94.00	100.20
200	190.00	186.00

Catfish (*Ictalurus punctatus*)		
Nominal boron concentration boron (ppm)	Measured boron concentration (ppm) – soft water (50 ppm $CaCO_3$)	Measured boron concentration (ppm) – hard water (200 ppm $CaCO_3$)
0.01	Not reported	Not reported
0.05	Not reported	Not reported
0.1	0.11	Not tested
0.5	0.49	0.53
0.75	Not tested	0.77
1	1.01	0.96
2.5	Not tested	2.33
5	5.42	4.90
7.5	7.43	7.40
10	10.00	9.43
25	24.90	25.10
50	51.40	48.30
75	Not tested	77.70
100	98.30	Not tested

150	151.00	140.00
200	177.00	Not tested
300	306.41	302.00

Goldfish (*Carassius auratus*)		
Nominal boron concentration boron (ppm)	Measured boron concentration (ppm) – soft water (50 ppm $CaCO_3$)	Measured boron concentration (ppm) – hard water (200 ppm $CaCO_3$)
0.05	Not reported	Not reported
0.1	0.1	0.12
0.5	0.49	0.47
1	0.90	0.90
5	5.20	4.50
7.5	7.00	6.80
10	9.20	8.33
25	22.50	32.00
50	48.70	51.30
100	108.00	96.70
200	188.70	191.00
300	288.00	290.00

Expressed in ppm boron at 4 days post-hatching, LC_1 values for trout, catfish, and goldfish were 0.1, 0.5, and 0.6 for boric acid in soft water and 0.001, 0.2, and 0.2 for boric acid in hard water, respectively.

Rainbow trout: Developmental stages of the trout were exposed for 28 days to boron concentrations ranging from 1 ppb to 200 ppm. Average hatching time was 24 days at 13-14°C. From 1 to 200 ppm boron, percent hatchability of trout eggs generally was inversely proportional to exposure level. At 1 ppm boron, hatchability varied from 94-99%. Treatment with low concentrations of boric acid gave more variable results, with 5-8% embryonic lethality occurring at boron concentrations as low as 0.01 ppm. High concentrations of boron were required to produce substantial levels of embryonic mortality. At 200 ppm, hatching frequencies were reduced to 55% and 65% for boric acid in soft and hard water, respectively. Using 50 ppm boron, egg hatchability varied from 77-82% for boric acid. Boric acid produced the highest frequencies of teratogenic survivors, particularly when used at a water hardness level of 200 ppm $CaCO_3$. In the latter case, 51% of those animals that survived 100 ppm boron were grossly defective, and frequencies dropped to 26, 11, and 5% at 1.0, 0.01, and 0.002 ppm boron, respectively. A high incidence of teratogenesis was observed over a broad range of exposure levels, varying from 200 to 1.0 ppm boron. Results were much more variable and less pronounced when boric acid was administered in soft water (50 ppm $CaCO_3$), with 27, 1, 21, and 5% of survivors bearing anomalies at exposure levels of 200, 50, 1.0, and 0.01 ppm boron.

In the trout bioassay, boron exposure level spanned a dilution range of 200,000 without achieving the full range of test responses. The test responses most characteristic of boron toxicity to embryonic and early juvenile stages of the rainbow trout may be summarized as follows: generally, high frequencies of both embryonic and post-embryonic mortality were recorded only at boron concentrations of 50 ppm or more. Embryonic mortality and teratogenesis were the principal boron-induced responses at 50 ppm or less. Though results with boric acid were variable, trout embryos suffered mortality and teratogenesis at frequencies of 10% or more at boron levels as low as 0.01 ppm, and 4-7% of test animals were affected by 0.001 ppm at 4 days post-hatching. While water hardness did not exert a profound influence on boron bioassays with trout, hard water generally increased embryonic lethality and teratogenesis, and soft water increased boron toxicity to post-hatched alevins. The fact that high concentrations (25-200 ppm) were required to consistently produce substantial impairment of test populations indicates that boron compounds are not highly toxic to trout embryos and alevins. However, compared to trace metals (e.g., cadmium and mercury), boric acid is unusual in that it exerts low-level embryopathic effects on trout over a wide span of exposure levels.

Channel catfish: Average hatching time was 5 days at 25-29 °C. Boron exposure levels ranged from 0.01-300 ppm in soft and hard water. Percent egg hatchability and percent normal survival at hatching and 4 days post-hatching gave good inverse correlations with boron concentration. Boron (300 ppm) produced lethality or teratogenesis at hatching in 100% of the experimental populations, and normal survival at 4 days post-hatching was only 0-2% at 200 ppm boron. Using boric acid in soft water, frequencies of normal survival at 4 days post-hatching increased to 56, 75, 95, and 99% at concentrations of 150, 10, 1.0, and 0.5 ppm boron, respectively. Normal survival was 100% at and below 0.1 ppm. Treating with boric acid in hard water, normal survival values at 4 days post-hatching were 9, 65, 86, and 98% at 75, 10, 1.0, and 0.01 ppm boron, respectively. Boric acid produced greater impairment of the test population when administered in hard water. Similar to results with trout, embryonic mortality and teratogenesis increased in hard water. However, differences were observed with post-hatched stages. Catfish fry were somewhat more sensitive to boron in hard water. As in the trout bioassay, boron concentrations of 50 ppm or more were required to produce high levels of post-hatched mortality.

However, catfish fry were somewhat more susceptible than were trout alevins to lower concentrations of boron.

The boron dilution ranges required to give test responses varying from 0-100% were approximately 3,000 and 30,000 for boric acid in soft and hard water, respectively. The effective dilution range increased with the order of toxicity. Catfish stages collectively were less sensitive to boron than trout stages by approximate factors of 200 and 5 for boric acid in hard and soft water, respectively. Differential sensitivity was greatest under conditions that proved most toxic to both species (e.g., boric acid in hard water).

Goldfish: Average hatching time was 3 days at 25-27 °C. Hatchability and normal survival gave good inverse correlations with boron concentration. Boron at 200 ppm produced complete lethality in all tests. Treating with boric acid in soft water, frequencies of normal survival at 4 days post-hatching were 4, 52, 94, and 98% for boron concentrations of 100, 50, 10, and 1 ppm. With hard water, normal survival averaged 325, 67, 85, and 98% for the same exposure levels.

As for trout, substantial levels of post-hatched mortality were found only at the higher boron concentrations, and post-hatched stages were somewhat more susceptible to boric acid in soft water. Unlike the trout and catfish, appreciable frequencies of teratogenesis occurred only at high exposure levels. Frequencies exceeding 10% were observed only at or above 100 ppm boron.

In all instances, normal post-hatched survival was 92% or more at and below 7.5 ppm boron, and there was a broad near-threshold range extending to 0.05 ppm boron at which low levels of embryonic mortality and/or teratogenesis consistently were observed.

The effective dilution range was approximately 6000 for boric acid. Goldfish were less sensitive than trout stages by approximate factors of 200 and 6 for boric acid in hard and soft water, respectively.

Reference: Birge, W. J. and J. A. Black (1977). NTIS PB-267085.

Leitritz, E. (1972). Trout and Salmon Culture, State of California, Dept. Fish and Game, Fish. Bull. #107 (cited in Birge and Black, 1977).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Acute Toxicity to Fish:

Supporting Data: Isopropyl Alcohol

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Exxon Corp. (1982). EG&G Report No. BP-82-7-71, TSCA Fiche OTS0510683.

Atlantic Richfield Company (1976). Industrial Bio-Test laboratories, Inc., IBT No. 621-08200 (February 3) (TSCA Fiche OTS0513281).

Exxon Corporation (1982). Bionomics Report #BW-82-7-1226 (July) (TSCA Fiche OTS0510679).

Mattson, V. R. et al. (1976) Ecol. Res. Ser. EPA-600/3-76-097 (AQ-0057190 through AQ-0057194).

Exxon Corporation (1982). EG&G, Bionomics Report #BW-82-7-1229 (July) (TSCA Fiche OTS0510684).

Wolverton, B. C. et al. (1970). Technical Report AFATL-TR-70-68, AD879811.

Brooke, L. T. et al. (eds.) (1984). Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*), pp. 69-74, Center for Lake Superior Environmental Studies, University of Wisconsin-Superior, Superior, WI.

Supporting Data: Boric Acid

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Office of Pesticide Programs (1995). Environmental Effects Database (EEDB), Environmental Fate and Effects Division, US EPA, Washington, DC (AQ-0198457 and AQ-0198458).

Office of Pesticide Programs (1995). Environmental Effects Database (EEDB), Environmental Fate and Effects Division, US EPA, Washington, DC (AQ-0198452 and AQ-0198453).

Procter and Gamble Company (n. d.). Unpublished Report (cited in IUCLID (2000). IUCLID DataSet, "Boric acid, crude natural, containing not more than 85% of H_3BO_3 calculated in the dry weight" (February 18)).

Procter and Gamble Company (1987). Report for the US EPA, Washington, DC (cited in IUCLID (2000). IUCLID DataSet, "Boric acid, crude natural, containing not more than 85% of H_3BO_3 calculated in the dry weight" (February 18)).

4.2 Acute Toxicity to Aquatic Invertebrates

No data for triisopropylborate exists, since the chemical rapidly hydrolyzes to boric acid and isopropanol. Therefore, for this robust summary, supporting data for the hydrolysis products are presented.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: **96-hour LC_{50}**

Species: *Mysidopsis bahia*, mysid shrimp

Value: 96-hour LC_{50} = 4050 ppm (95% confidence limits, 2530-5030 ppm)

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Mysid shrimp (3-4 days old) were exposed to nominal concentrations of 0, 625, 1250, 2500, 5000, 10,000 or 20,000 ppm in a static 96-hour acute toxicity test. Ten shrimp were tested per dish and treatments were duplicated, resulting in 20 shrimp per treatment. There was no aeration. Dissolved oxygen (DO) concentrations were $\geq$87% of saturation at initiation of the test. Shrimp were fed live brine shrimp nauplii on days 0 and 2 of the test.

Test concentrations were prepared by adding appropriate volumes of the test substance to the seawater in the test containers. The test containers were then covered with aluminum foil and stirred for 4 hours. The shrimp were added to the test containers when the temperature decreased to 23°C. A concurrent seawater control was conducted.

Water samples for chemical analysis were taken from each test container at the initiation and termination of the test. If all shrimp died in a test container prior to termination of the test, the water sample was taken at that time. All water samples were refrigerated until shipment for analysis. No additional details regarding water chemistry parameters were reported.

Based on the results of the test, the LC_{50} values were calculated using the moving average angle method.

GLP: Unknown

Test Substance: Isopropanol, purity not reported

Results: After 3 hours of exposure, mortality was 0% in all test concentrations. After 96 hours of exposure, mortality was 5, 5, 5, 5, 55, 100, and 100 at 0, 625, 1250, 2500, 5000, 10,000, and 20,000 ppm, respectively. The 24- 48-, and 72-hour LC_{50}s were 5910, 4960, and 4170 ppm, respectively. Additional data, including effects per concentration were either not reported or the information could not be clearly discerned on the TSCA fiche.

The test salinity and temperature were 20% and 21-23°C. The dissolved oxygen concentrations and pH remained within acceptable ranges throughout the test. After 96 hours of exposure, dissolved oxygen concentrations were >87% of saturation in all test concentrations and the control. Initial pH was 8.3-8.5 in the control and all test concentrations. The pH after 96 hours of exposure was 7.9-8.0 in the control and all test concentrations with surviving shrimp.

Reference: Exxon Corp. (1982). EG&G Bionomics Report No. BP-82-7-69, TSCA Fiche OTS0510681.

Reliability: Medium because a suboptimal study design (nominal test concentrations) was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: **24-hour EC_{50}**

Species: *Daphnia magna*

Value: 159,000 µmol/L (29,906 mg/L)

Method: Test procedures were based on OECD Guideline 202. The 24-hour EC_{50} was calculated by the Trimmed Spearman-Karber method. No additional details were reported, including concentrations tested, test system type, number of organisms per concentration, duplicate experiments, loading rate, controls, or water chemistry parameters.

GLP: Unknown

Test Substance: Isopropanol, purity >97%

Results: No additional data regarding mortality and effects per concentration were reported.

Reference: Calleja, M. C. et al. (1994). Arch. Environ. Contam. Toxicol., 26:69-78.

Reliability: Medium because a suboptimal study design (nominal test concentrations) was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: **16-day log NOEC (growth)**

Species: *Daphnia magna*

Value: 3.37 µmol/L (0.63 mg/L)

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Daphnia (<1 day old) were exposed to the test substance (concentrations not reported) for 16 days (3-4 broods) in 2 duplicate experiments with 15 organisms each. The test volume was 1 L/group, and the test medium was Dutch standard water at a hardness of ca. 1 mmol/L. The static test had a ratio between the concentrations of the toxicant tested of 1.8, and the renewing rate was 3 times/week. *Daphnia* were fed *Chlorella* sp. during the test.

At the start of the experiments and after 16 days, the lengths of 30 daphnids were measured. The NOEC on growth was defined as the highest concentration that did not result in a significant reduction in growth (tested with Student's t-test).

During the test, the actual concentrations were determined once for the lowest and highest concentration just before and after renewal of the test solutions in the semi-static experiments. Additional details, including number of organisms per concentration, loading rate, and control information were not reported.

GLP: Unknown

Test Substance: Isopropanol, purity not reported

Results: The chemical analyses showed that between 80 and 110% actually was present in the test solutions. The percentage was a mean value of analyses from samples out of the duplicate experiments that were taken just before and after the test solutions were renewed. The NOEC value was not corrected for the measured concentration, since this had only a slight influence on the calculated QSARs.

Reference: Hermens, J. et al. (1985). Aquatic Toxciol., 6:209-217.
Hermens, J. et al. (1984). Aquatic Toxicol., 5:143-154.

Reliability: High because a scientifically defensible or guideline study was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: **16-day log EC_{50} (reproduction)**

Species: *Daphnia magna*

Value: 4.73 µmol/L (0.89 mg/L)

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Daphnia (<1 day old) were exposed to the test substance until the control daphnids had produced 4 broods. The test volume was 1 L/group, and the test medium was Dutch standard water at a hardness of ca. 1 mmol/L. The static test had a ratio between the concentrations of the toxicant tested of 1.8, and the renewing rate was 3 times/week. *Daphnia* were fed *Chlorella* sp. during the test.

Fifteen daphnids were exposed to each test concentration (concentrations not reported) in duplicate experiments. In the semistatic tests on single compounds, the actual concentrations were determined once for the lowest and highest concentration (in duplicate) just after and before renewal of the test solutions. The test substance was analyzed using gas-liquid chromatography. No additional details regarding loading rate, controls, or water chemistry parameters were reported.

The NOEC on reproduction was defined as the highest concentration that did not result in a reduction of reproduction compared with the control. The EC_{50} values were calculated by the method of Litchfield and Wilcoxon. The NOEC on growth was defined as the highest concentration that did not result in a significant reduction in growth compared with the control.

GLP: Unknown

Test Substance: Isopropanol, purity not reported

Results: The log NOEC for reproduction and growth were 4.37 and 4.11 μmol/L, respectively. No additional data, including mortality and effects per concentration were reported.

Determined concentrations were 80-104% of the calculated amount. The percentages were mean values of at least 4 determinations. The average decrease in concentration during the tests was 9%, with a maximum of 26%. The NOEC and EC_{50} values were not corrected for the measured losses because this would have only a slight influence on the QSARs.

Reference: De Wolf, W. et al. (1988). Aquatic Toxicol., 12:39-49.

Hermens, J. et al. (1984). Aquatic Toxicol., 5:143-154.

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: **48-hour LC_{50}**
21-day LC_{50}

Species: *Daphnia magna*

Value: 48-hour LC_{50} = 133 mg/L, as boron (95% confidence interval, 115-153 mg/L)

21-day LC_{50} = 52.2 mg/L, as boron (95% confidence interval, 42.6-66.7 mg/L)

Method: Acute toxicity testing procedures were based on the guidelines of the ASTM Subcommittee on Safety to Aquatic Organisms, Standard E 729-80.

Lake Huron water was used to culture daphnids and as test dilution water. The water was carbon-filtered, UV-irradiated, and adjusted to a hardness of approximately 170 mg/L as $CaCO_3$. The water was then autoclaved at 120 °C and 124.1 kPa for 35 minutes.

Acute Toxicity Test: The static acute test was conducted in 250 mL beakers to which 200 mL of the appropriate amount of test substance and water was added. The test consisted of exposing 3 replicate groups of 10 neonates to each of 6 nominal concentrations (54, 91, 151, 252, 420, and 700 mg/L as boron) of the test substance and control. The loading rate of the daphnids was not reported. In addition, an extra beaker was set at the high, medium, low, and control concentrations to avoid the risk of contamination while taking dissolved oxygen, pH, and temperature measurements. The test beakers were placed in a temperature-controlled environmental chamber set at 20±1 °C and a photoperiod of 16 hours light: 8 hours dark. The duration of the test was 48 hours. Mortality, as well as dissolved oxygen, pH, and temperature were recorded after 24 and 48 hours of exposure. Daphnids were not fed, nor were the solutions aerated during the test.

Chronic Toxicity Test: A static renewal procedure, with batchwise replacement of test and control solutions at regular intervals (Monday, Wednesday, and Friday) was used in the chronic test. The test vessels were 600 mL glass beakers. Each beaker contained a mesh stainless steel platform and 5 glass tubes with nylon mesh bottoms. The tubes were placed on the platform to allow water circulation. Each test beaker contained 500 mL of the appropriate amounts of test material, food, and water. During the test the solutions were gently aerated to achieve 90 to 105% saturation. There were 4 replicates for each test concentration and the control, resulting in 5 daphnids per replicate or a total of 20 organisms per concentration. The daphnids were fed *S. capricornutum* during the test. The test beakers were placed in a temperature-controlled environmental chamber set at 20±1 °C and a photoperiod of 16 hours light: 8 hours dark. The duration of the study was 21 days. The chronic study began by placing one neonate in each tube, where the daphnid remained for the entire study. Each Monday, Wednesday, and Friday the young produced by each adult were counted and discarded, and adult survival was recorded. In addition, on the same days, the dissolved oxygen, pH, and temperature in each test concentration and the control were measured and recorded. After enumeration of the young, the adults were transferred to clean beakers containing fresh test and control solutions, in addition to a new supply of food. The boric acid test concentrations used for the chronic test were 7, 14, 28, 56, and 105 mg/L as boron. The test concentrations were verified using the carmine method. On each Monday, Wednesday, and Friday analyses were performed on all replicates from 1 particular test concentration and on 1 replicate from each remaining test concentration and control. The boron concentrations were also analyzed in renewed solutions (time zero) and the same test solution prior to the next renewal to determine the stability of the test substance.

The LC_{50} value for the acute toxicity test was based on nominal concentrations, but the LC_{50} value for the chronic toxicity test was based on measured concentrations. Finney's method of probit analysis or the moving average method was used to calculate the LC_{50} values. Data from the chronic portion of the study were analyzed using a two-tailed Dunnett's t test. Mean comparisons between test and control concentrations were performed on the mean number of broods per daphnid, mean total young per daphnid, mean brood size per daphnid, and mean length, in effort to estimate the maximum acceptable toxicant concentration (MATC).

GLP: Unknown

Test Substance: Boric acid, purity not reported

Results: During the study, pH was 8.1±0.1, conductivity was 290±31 µmhos/cm, hardness was 148±7 mg/L as $CaCO_3$, and alkalinity was 58±5 mg/L as $CaCO_3$. The boron concentration in the water was 0.4±0.1 mg/L. Lake Huron contains about 12 µg/L boron.

Acute Toxicity Test: The no-kill level was <54 mg/L and the 100% kill concentration was 420 mg/L. There was 7% control mortality during the 48-hour test. Mortality and effects per concentration were not reported. Dissolved oxygen concentrations throughout the test were greater than 60% saturation and the pH ranged from 6.7 to 8.1. Temperatures ranged from 20.1 to 20.7 °C.

Chronic Toxicity Test: The mean boron concentration was 0, 6.4, 13.6, 29.4, and 59.3 at 0, 7, 14, 28, and 56 mg/L, respectively. The means of the analyzed concentrations ranged from 91.4 to 106% of the nominal concentrations. The boron concentrations in the renewed test solutions (time zero) and for the same test solutions prior to the next renewal were not significantly different, thus attesting to the stability of the test substance over the renewal period. Throughout the chronic test the dissolved oxygen and temperature ranged from 7.3-8.0 mg/L and 19.5-20.5 °C, respectively. Mortality during the 21-day test was 0, 0, 10, 5, and 40% at 0, 7, 14, 28, and 56 mg/L, respectively. No data were available for daphnids exposed to the highest concentration of boric acid (105 mg/L as boron) because none survived to reproductive age. Time to first reproduction was not affected by the test concentrations. The mean number of broods per daphnid, mean total young per daphnid, mean brood size per daphnid, and mean size all differed significantly from control at 13.6 mg/L. It appeared that the most biologically, as well as statistically, important endpoints for this study were those associated with reproduction and growth. Therefore, determination of the MATC was based on the endpoints of mean total young per replicate, mean brood size, and mean size. The MATC of boric acid was estimated to lie between 6.4 and 13.6 mg/L as boron.

Reference: Gersich, G. M. (1984). Environ. Toxciol. Chem., 3:89-94.

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: **8-day EC_{50}**

Species: *Ceriodaphnia dubia*

Value: >100 mg/L

Method: The definitive toxicity test was performed according to U.S. Environmental Protection Agency Method 1002.0, “Short Term Method for Estimating the Chronic Toxicity of Effluents and Receiving Waters to Freshwater Organisms.

Ceriodaphnia Survival and Reproduction Test," EPA/600/4-85/014.

The test was performed under static, renewal conditions at nominal concentrations of 0, 6.25, 12.5, 25, 50, and 100 mg/L. The test was conducted at a target temperature of 25±1 °C. Stock solutions were prepared every day during the test. The test media was renewed in each test vessel daily. Dilution water was bottled drinking water adjusted to a hardness of approximately 100 mg/L as $CaCO_3$. Water was stored in a glass tank where it was temperature adjusted and aerated.

Ten neonates, less than 24 hours old at test initiation, were indiscriminately distributed among 10 replicates of each concentration (1 per vessel). Adults were transferred to fresh dilution water every 1-8 days. The number of duplicate tests and loading rate were not reported. The culture was maintained in a 4-L glass jar that was filled to approximately 50-90% capacity. The culture was supplied with a yeast/trout chow mix and freshwater alga daily before the start of the test.

Test vessels were arranged in an incubator. A 16-hour light and 8-hour dark photoperiod was automatically maintained with cool-white fluorescent lights. Aeration was not used.

The number of surviving adults and the occurrence of sub lethal effects (immobilization, loss of equilibrium, erratic swimming, loss of reflex, excitability, discoloration, or change in behavior) were determined visually and recorded at test start and every 24 hours. The young produced by each adult were counted and removed daily after the onset of reproduction.

Dissolved oxygen, pH, conductivity, and temperature were measured and recorded daily before and after media renewal in a composite of media from each test chamber. The hardness and alkalinity of the dilution water control and the highest tested concentration were measured and recorded daily.

All calculations were performed using nominal concentrations of test substance. Survival of first generation adults was not statistically analyzed and the EC_{50} could not be determined because 100% survival occurred at all tested concentrations. The number of young per adult was statistically analyzed. A Chi-square test was used to determine that data were normally distributed, and Bartlett's test was used to determine that variances were homogeneous. Because the assumption of homogeneity of variances was met, a parametric one-way analysis of variance followed by Dunnett's test was used to compare treatment with control means. Data were not transformed prior to statistical analyses.

GLP: Yes

Test Substance: Boric acid, purity >99%

Results: A screening test was performed for 48-hours to nominal concentrations of 0, 0.10, 1, 10, 100, and 1000 mg/L. At the end of the test there was 0% survival at 1000 mg/L, 10% survival at 100 mg/L, and 100% survival at all lower concentrations.

Insoluble material was not observed in any test vessel during the test. Control survival was 100% at test end and first-generation adults produced an average of 17.4 young during the 3-brood study.

Water quality parameters were within acceptable limits throughout the study. Dissolved oxygen concentrations were always above 7.8 mg/L. During the test, the mean temperature was 24.4°C, the mean conductivity was 350 µmhos/cm, and the pH ranged from 7.1 to 8.3. Hardness ranged from 88 to 100 mg/L in control vessels and from 88 to 108 mg/L in vessels containing 100 mg/L of the test substance. Alkalinity ranged from 16 to 21 mg/L in control vessels and from 16 to 23 mg/L in vessels containing 100 mg/L of the test substance.

The percentage of surviving adults was not significantly reduced at any tested concentration, and sublethal effects were not observed at any concentration. The mean number of young per surviving adult was significantly lower than the control at the 3 highest tested concentrations (25, 50, and 100 mg/L).

The most sensitive biological endpoint was production of young. The NOEC, LOEC, and MATC were12.5, 25, and 17.7 mg/L, respectively. The 8-day EC_{50} was >100 mg/L. Because no adults were affected, the EC_{50} response criteria was death.

Reference: DuPont Co. (1993). Unpublished Data, Haskell Laboratory Report HLO-418-93, "Chronic Toxicity to *Ceriodaphnia dubia*" (June 2).

Reliability: Medium because a suboptimal study design (nominal test concentrations) was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: **14-day NOEL**

Species: *Daphnia magna*

Value: Approximately 14 mg/L

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

All daphnids were cultured and tested in Lake Huron water, which was adjusted to a hardness of approximately 170 mg/L as $CaCO_3$, prior to autoclaving. The water was autoclaved at 121 C and 124 kPa for 35 minutes. Daphnids were fed a diet of *Selenastrum capricornutum* Printz.

The chronic tests were conducted in a manner similar to that reported by Gerisch, 1984 and Gerish et al., 1984. The studies were designed to use a static renewal procedure with batch-wise replacement of the test and control solutions on a Monday, Wednesday, and Friday basis. Two chronic daphnid studies were conducted. The test vessels were 600 mL glass beakers, each containing 5 glass tubes with wire mesh bottoms. The tubes were supported off the bottom of the beaker with a mesh stainless steel platform. During the studies, each beaker contained the appropriate amount of food, dilution water, and test material made up to a 500 mL volume. The test organisms were fed *Selenastrum capricornutum*. The beakers were held in a temperature controlled environmental chamber set at 24±2 °C and a photoperiod of 16 hours daylight/ 8 hours darkness.

The chronic tests began by placing 1 neonate daphnid in each uniquely labeled tube. The daphnids remained in their respectively labeled tubes for the duration of the study. Each test and control concentration had 4 replicates, resulting in 20 daphnids being exposed to each concentration. Two tests were performed. The duration of each test was 14 days. The critical endpoints were associated with reproduction, growth, and survival. The reproductive endpoint was obtained by hand counting the neonates on a Monday, Wednesday, and Friday basis. Growth was calculated by determining the dry weight of the surviving adult organisms at the tests end. Survival data were collected every Monday, Wednesday, and Friday. Additionally, pH, dissolved oxygen, and temperature were measured and recorded on each renewal day.

Samples from the boric acid chronic static renewal tests were analyzed, using an appropriate high performance liquid chromatography method. On each Monday, Wednesday, and Friday during all studies, analyses were performed on a replicate from each test concentration and the control.

Data derived from the studies were analyzed by a one-tailed Dunnett's test. The Dunnett's procedure used simultaneously tested for heterogeneity of variances using Bartlett's test. If the variances were heterogeneous, the Wilcoxon signed rank test was used to compare the means. Mean comparisons between test and control concentrations were performed on percent survival, meant total young/adult, mean brood size/adult, and mean dry weight/adult to estimate the MATC.

GLP: Unknown

Test Substance: Boric acid, purity 99.5%

Results: During both boric acid studies, all analyzed concentrations were within a range of 98.5 and 111.4% of nominal.

Interpretation of the chronic data for boric acid indicates that the MATC is between 13.8 and 28.1 mg/L for Test I and between 14.3 and 28.9 mg/L for Test II. Expressing the MATC as a geometric mean of these concentrations for Tests I and II resulted in MATC's of 19.7 and 20.3 mg/L, respectively. The NOEL for both studies was approximately 14 mg/L. The estimation of the MATC's was based on data associated with survival, reproduction, and growth. These endpoints all significantly differed from the controls at the 28 mg/L concentration. No other toxic effects were observed during the studies. During both studies, >48% of the healthy organisms had first broods on day 6.

Additional details can be found in the table below:

Mean analyzed concentration (mg/L)	Survival (%)	Mean total young/adult	Mean brood size/adult	Mean dry weight/adult (µg)
TEST I:				
0	100	72.2	22.2	397.5
7.4	100	74.4	22.6	378.5
13.8	95	70.8	22.4	397.3
28.1	70	14.9	9.3	54.8
57.4	0	0	0	0

107.4	0	0	0	0
TEST II:				
0	100	72.6	22.7	400
7.8	100	73.0	22.1	396.5
14.3	100	69.4	22.4	345.5
28.9	65	16.6	9.8	73.3
60	0	0	0	0
113.2	0	0	0	0

During the two 14-day studies with boric acid, no mortality was observed in the controls. The dissolved oxygen measurements were >90% saturation during both tests (range 8.3 to 8.8 mg/L). The pH and temperature measurements ranged from 7.3 to 8.2 and 23.0 to 25.2°C, respectively.

Reference:

Gersich, F. M. and D. P. Milazzo (1990). Arch. Environ. Contam. Toxicol., 19:72-76.

Gerish, F. M. (1984). Environ. Toxicol. Chem., 3:89-94 (cited in Gersich, F. M. and D. P. Milazzo (1990). Arch. Environ. Contam. Toxicol., 19:72-76).

Gerisch, F. M. et al. (1984). Bull. Environ. Contam. Toxicol., 32:497-502 (cited in Gersich, F. M. and D. P. Milazzo (1990). Arch. Environ. Contam. Toxicol., 19:72-76).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Acute Toxicity to Invertebrates:

Supporting Data: Isopropanol Alcohol

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Blackman, R. A. A. (1975). Mar. Pollut. Bull., 1:116-118.

Lilius, H. et al. (1994). Aquatic Toxicol., 30:47-60.

Lilius, H. et al. (1994). Environ. Toxicol. Chem., 14(12):2085-1088.

Bringmann, G. and R. Kühn (1982). Z. Wasser Abwasser Forsch., 15(1):1-6.

Bringmann, G. and R. Kühn (1977). Z. Wasser Abwasser Forsch., 10(5):161-166.

McCauley, D. J. (n. d.). Data, Wisconsin Department of Natural Resources, Madison, WI (cited in Vaishnav, D. D. and E. T. Korthals (1990). Arch. Environ. Contam. Toxicol., 19:624-628).

Supporting Data: Boric Acid

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Dow Chemical Co. (2000). TSCA Fiche OTS0518450.

Office of Pesticide Programs (1995). Environmental Effects Database (EEDB), Environmental Fate and Effects Division, US EPA, Washington, DC (AQ-0198454 through AQ-0198456 and AQ-0200581).

4.3 Toxicity to Aquatic Plants

No data for triisopropylborate exists, since the chemical rapidly hydrolyzes to boric acid and isopropanol. Therefore, for this robust summary, supporting data for the hydrolysis products are presented.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: **5-Day Algistatic Concentration (AC)**

Species: *Selenastrum capricornutum*, green algae

Value: 54,294 ppm (95% confidence limits: 41,565-70,922 ppm)

Method: Test procedures were based on "A Method for Measuring Algal Toxicity and Its Application to the Safety Assessment of New Chemicals (Payne and Hall, 1979), and the U.S. Environmental Protection Agency (1978).

A primary stock solution was prepared by adding a weighed amount of test material to algal growth medium. The test concentrations were then prepared by adding appropriate volumes of the primary stock solution to the test containers. Test conditions included a temperature of 24±1 °C and light intensity of approximately 4,000 lux. Algae were tested at nominal concentrations of 3125, 6250, 12,500, 25,000, and 50,000 mg/L for five days. The effect criterion was change in cell numbers.

GLP: Unknown

Test Substance: Isopropanol, purity 100% active ingredient

Results: After 5 days of exposure, the percentage change of cell numbers in exposed cultures as compared to the control was from +121% at 3,125 ppm to –99% in cultures exposed to 50,000 ppm. Measurements of *in vivo* chlorophyll *a* showed a growth-concentration response similar to the observed effect based on cell numbers. After 5 days of exposure, the percentage change of relative fluorescence units was from +17 in cultures exposed to 3,125 ppm to –100% in cultures exposed to 50,000 ppm. Based on cell numbers, the growth of cultures previously exposed to 50,000 ppm was approximately one-half (-47%) that of the controls during a 9-day recovery period in test material-free medium, indicating at least a partial algicidal effect. Measurements of *in vivo* chlorophyll *a* showed a growth response similar to the observed effect based on cell numbers during the recovery phase. After 9 days of recovery, the percentage decrease was 50% in the previous 50,000 ppm exposure concentration when compared to the growth medium control.

Reference: Exxon Corp. (1983). EG&G Report No. BP-83-2-9, TSCA Fiche OTS0510685.

Reliability: Medium because a suboptimal study design (nominal test concentrations) was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: **Boron Tolerance and Accumulation**

Species: *Lemna minor* L., duckweed

Value: 7-day NOEC > 20 μg/mL

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Cultures of duckweed were maintained axenically in F-medium, which was adjusted to pH 5. The plants were grown in continuous 100 μE/m^2/s mixed cool-white fluorescent and incandescent light in the 400 to 700 nm region at 25±2 °C, and transferred as three-frond clones of approximately the same age to sterile F-medium incorporating boric acid (10 to 20 μg/mL). Despite the high pK's for this weak acid, it was in all cases soluble. Replicate cultures (12-15) were incubated for a typical 7-day experiment.

Daily frond number counts for each replicate were made and the change in frond number was calculated. The frond doubling time was calculated using a procedure to ensure growth rate only during the steady-state phase was measured – lag period effects were avoided by excluding data of day 1 and stationary phase effects were not apparent during the treatment period.

Plants were harvested and washed, towel-dried, weighed, and hand homogenized. The homogenates were centrifuged and aliquots of the supernatant assayed for boron. The insoluble pellet was digested, diluted, and centrifuged, and protein determined in the supernatant by the Folin method. Boron was determined colorimetrically in the soluble extract after reaction with Azomethine-H. Azomethine-H assays were run in duplicate on triplicate plant samples of each treatment comprising an experiment, and each experiment repeated at least twice.

GLP: Unknown

Test Substance: Boric acid, purity not reported

Results: *Lemna minor* tolerated between 10 and 20 µg/mL elemental boron in the growth medium at pH 5.0 without being inhibited. Plants grown for 6 days in 50 or 100 µg/mL boron in the medium partially recovered control rates of growth during 5 days incubation in control medium; 200 µg/mL boron was toxic beginning at about 3 days of exposure.

Reference: Frick, H. (1985). J. Plant Nutr., 8(12):1123-1129.

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Acute Toxicity to Aquatic Plants:

Supporting Data: Isopropyl Alcohol

Data from this additional sources support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Adams, V. D. et al. (1975). NTIS PB250730.

Supporting Data: Boric Acid

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Wong, P. K. and C. K. Wong (1990). Bull. Environ. Contam. Toxicol., 45:752-759.

Anita, N. J. and J. Y. Cheng (1975). J. Fish. Res. Board. Can., 32:2487-2494 (cited in IUCLID (2000). IUCLID DataSet, "Boric acid, crude natural, containing not more than 85% of H_3BO_3 calculated in the dry weight" (February 18)).

Nobel, W. (1981). Angewandte Botanik, 55:501-514 (AQ-0066917 through AQ-0066924).

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type: **Oral LD_{50}**

Species/Strain: Male rats/ChR-CD

Value: 8,126 mg/kg (95% confidence limits, 7828-8549 mg/kg)

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test substance, as received, was administered by intragastric intubation in single doses of 7000, 7500, 8000, and 9000 mg/kg, to 4 groups of young adult male rats, 10 animals per dose level. Survivors were sacrificed without pathologic examination 14 days later. The LD_{50} was calculated from mortality data using the method of D. J. Finney.

GLP: No

Test Substance: Triisopropylborate, actual purity or presence of constituents not reported (test substance reported as "pure")

Results: Mortality was 0/10, 1/10, 5/10, and 9/10 at 7000, 7500, 8000, and 9000 mg/kg, respectively. All mortality occurred 1-3 days after dosing. Weight loss occurred 1-3 days after dosing at all levels tested. Test days that clinical signs were observed are included in the table below.

Dose (mg/kg):	7000	7500	8000	9000
Clinical Sign:				
Alopecia	-[a]	-	2	-
Belly to cage posture	0	0	0-2	0
Chromodacryorrhea	1-3	1-3	1,3-5	3-6,8
Diarrhea	2-3	2-3	2-5	-
Exophthalmos	3	-	-	-
Labored breathing	-	1	-	1-2
Lacrimation	-	1	-	0-2
Lethargic	-	0	-	3
Moribund	-	1	-	1-2
Piloerection	2-5,12	2-3,8	4-5,10	14
Prostration	0	0,2	0	-
Rapid breathing	1	0	1	0,4
Stained nose/face/mouth	-	-	1-3	1-3
Stained perineal	-	-	3	-

Unkempt fur	2	8	-	5-6
Weakness	1	-	1	-
[a] Clinical sign was not observed in any rat at this dose level.				

Reference: DuPont Co. (1978). Unpublished Data, Haskell Laboratory Report No. 491-78, "Oral LD_{50} Test" (August 25).

Reliability: High because a scientifically defensible or guideline method was used.

Additional Reference for Acute Oral Toxicity:

Data from this additional source support the rat LD_{50} study results summarized above. This study was not chosen for detailed summarization because the data did not substantially add to this database.

DuPont Co. (1975). Unpublished Data, Haskell Laboratory Report No. 512-75, "Acute Oral Test" (August 15).

Type: **Oral LD_{50}**

Species/Strain: Mice/Swiss

Value: 2500 mg/kg (2.5 mL/kg)

Method: No specific test guideline was reported.

The acute oral toxicity of the test substance was determined by forced feeding of the test substance to adult Swiss mice. From the dose that killed 50% of the animals during a 10-day observation period and the weight of the animals, the LD_{50} dose was calculated. No information regarding vehicle, gender, number of mice per dose level, dose levels tested, or statistical methods was reported.

GLP: No

Test Substance: Triisopropylborate, purity not reported

Results: No additional data regarding mortality and effects per concentration were reported.

Reference: Adams, R. M. (ed.) (1964). Boron, Metallo-boron Compounds, and Boranes, pp. 693-737, Interscience Publishers, New York (also cited in RTECS/ED5950000).

Reliability: Not assignable because limited study information was available.

Additional Reference for Acute Oral Toxicity:

Data from this additional source support the rat LD_{50} study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1975). Unpublished Data, Haskell Laboratory Report No. 512-75, "Acute Oral Test" (August 15).

Type: **Inhalation Toxicity:** No Data.

Type: **Dermal Toxicity:** No Data.

Type: **Dermal Irritation**

Species/Strain: Male guinea pigs/Albino

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test for primary irritation was conducted by applying and lightly rubbing in one drop (approximately 0.05 mL) of the test substance as received and as a 25% solution (vol/vol) in distilled water on the shaved, intact shoulder skin of 10 male albino guinea pigs (initial average weight 441 g).

GLP: No

Test Substance: Triisopropylborate, purity not reported

Results: The test substance did not produce primary irritation in any guinea pig tested at 100% or 25%. One guinea pig in the 100% group died due to non-test substance-related causes.

Reference: DuPont Co. (1975). Unpublished Data, Haskell Laboratory Report No. 501-75, "Primary Skin Irritation and Sensitization Tests on Guinea Pigs" (August 28).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Dermal Irritation: None Found.

Type: **Dermal Sensitization**

Species/Strain: Male guinea pigs/Albino

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test for primary irritation was conducted by applying and lightly rubbing in one drop (approximately 0.05 mL) each of the test substance as received and as a 25% solution (vol/vol) in distilled water on the shaved, intact shoulder skin of 10 male albino guinea pigs (initial average weight 441 g). To test for the sensitization potential, a series of 4 sacral intradermal injections was given, 1 each week over a 3-week period, which consisted of 0.1 mL of a 1% solution (vol/vol) of the test substance in physiological saline. Following a 2-week rest period, the test animals were challenged for sensitization by applying, and lightly rubbing in, 1 drop (approximately 0.05 mL) each of the material as received and as a 25% solution (vol/vol) in distilled water on the shaved intact shoulder skin. A group of 10 previously unexposed guinea pigs (average weight 664 g) received similar applications at the time of challenge to provide a direct comparison of the challenge reactions on skin of similar age.

GLP: No

Test Substance: Triisopropylborate, purity not reported

Results: The test substance did not produce primary irritation or sensitization in any guinea pig tested at 100% or 25%. One guinea pig in the 100% group died due to non-test substance-related causes.

Reference: DuPont Co. (1975). Unpublished Data, Haskell Laboratory Report No. 501-75, "Primary Skin Irritation and Sensitization Tests on Guinea Pigs" (August 28).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Dermal Sensitization: None Found.

Type: **Eye Irritation**

Species/Strain: Rabbits/Albino

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

One-tenth milliliter of the undiluted test substance was placed into the right conjunctival sac of each of 2 albino rabbits. After 20 seconds, 1 treated eye was washed with tap water for 1-minute. The treated eye of the other rabbit was not washed. Observations of the cornea, iris, and conjunctiva were made with a hand-slit lamp at 1 and 4-hours, and at 1, 2, and 3 days. Fluorescein stain and a biomicroscope were used at examinations after the day of treatment.

GLP: No

Test Substance: Triisopropylborate, purity not reported

Results: The test substance produced no corneal, iritic, or conjunctival effects in the rabbit eye. Both treated eyes were normal at 1 hour.

Reference: DuPont Co. (1975). Unpublished Data, Haskell Laboratory Report No. 500-75, "Eye Irritation Test in Rabbits" (August 28).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Eye Irritation: None Found.

Type:	**Eye Irritation**
Species/Strain:	Rabbits/Strain not reported
Method:	No specific test guideline was reported. A dose consisting of 100 mg of the undiluted liquid was placed in the conjunctival sac of the eye. Eyelids were held together for at least 1 minute. Observations were made for at least 1 week following dosing.
GLP:	No
Test Substance:	Triisopropylborate, purity not reported
Results:	The test substance produced mild eye irritation in rabbits.
Reference:	Adams, R. M. (ed.) (1964). Boron, Metallo-boron Compounds, and Boranes, pp. 693-737, Interscience Publishers, New York (also cited in RTECS/ED5950000).
Reliability:	Not assignable because limited study information was available.

Additional References for Eye Irritation: None Found.

5.2 Repeated Dose Toxicity

No data for triisopropylborate exists, since the chemical rapidly hydrolyzes to boric acid and isopropanol. Therefore, for this robust summary, supporting data for the hydrolysis products are presented.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type:	Oral – Feed
Species/Strain:	Mice/B6C3F$_1$
Frequency of Treatment:	Daily
Method:	14-Day Study #1: The 14-day studies were part of a larger study involving exposure to boric acid in feed for 14 days, 13 weeks or 2 years. Male (n=5) and female (n=5) B6C3F$_1$ mice per group were exposed to boric acid in feed for 14 days. Boric acid doses were 0, 0.06, 0.12, 0.24, 0.49 and 0.98%. Animals were weighed on Days 1, 7 and 15. A necropsy was performed on all animals. 14-Day Study #2: Another 14-day study was conducted. Male (n=5) and female (n=5) B6C3F$_1$ mice per group were exposed 0, 0.62, 1.25, 2.5, 5.0 and 10%. Animals were weighed on Days 1, 7 and 15. A necropsy was performed on all animals
GLP:	Not determined
Test Substance:	Boric Acid, 99.7% pure.
Results:	14-Day Study #1: No mortality was observed. Five of five males and one of the females 0.98% (9,800 ppm) either lost weight or gained no weight. Final mean body weights of mice that received 0.49% were not adversely affected. No compound-related gross or microscopic pathologic effects were observed. The researchers considered this study to be inadequate and an additional 14-day study was conducted at higher doses to better characterize the 14-day toxicity of boric acid. 14-Day Study #2: In this study, mortality increased proportionally for both sexes as the dose increased. Mortality was observed in dose groups as low as 2.5% (1 of the 5 males) and as early as 7 days of exposure. Body weights were depressed more than 10% below controls in the higher dose groups of both sexes. No compound-related effect on feed consumption was observed. Hyperplasia and/or dysplasia of the forestomach was seen in 3/5 males and 2/5 females that received 25,000 ppm, 2/4 males and 2/3 females that received 50,000 ppm, and 4/4 males and 2/2

	females that received 100,000 ppm.
Reference:	NTP (1987) U.S. National Toxicology Program: Toxicology and carcinogenesis studies of boric acid (CAS No. 10043-35-3) in B6C3F1 mice (feed studies). NTP TR 324. DHHS (NIH) Pub. No. 88-2580. NTP, Research Triangle Park, NC (1987).
Reliability:	Not determined.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type:	Oral – Feed
Species/Strain:	Mice/B6C3F_1
Frequency of Treatment:	Daily for 13 weeks
Method:	The 13-week study was part of a larger study involving exposure to boric acid in feed for 14 days, 13 weeks or 2 years. Male (n=10) and female (n=10) B6C3F_1 mice were exposed to boric acid in feed 13 weeks. Doses were 0, 0.12, 0.25, 0.5, 1 and 2%. The effects studied were mortality, clinical signs of toxicity, food consumption, body weight, and histopathology of selected tissues.
GLP:	Yes
Test Substance:	Boric Acid, 99.7% pure.
Results:	Mortality was only observed in the two highest dose groups in male mice (1 of 10 in the 1% group and 8 of 10 in the 2% group) and 6 of 10 females in highest dose group (2%) in females. High dose animals (dose not given) showed signs of toxicity. Body weights of both sexes were about 8 to 23% below those of controls and occurred in the 0.50% and higher dose groups. Minimal to mild extramedullary hematopoiesis in spleens of both sexes was a common occurrence in all dose groups. The most severe lesion observed was testicular degeneration or atrophy of the seminiferous tubules in male mice in the 0.50 to 2.0% dose groups.
Reference:	NTP (1987) U.S. National Toxicology Program: Toxicology and carcinogenesis studies of boric acid (CAS No. 10043-35-3) in B6C3F1 mice (feed studies). NTP TR 324. DHHS (NIH) Pub. No. 88-2580. NTP, Research Triangle Park, NC (1987).
Reliability:	High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type:	Oral – Feed
Species/Strain:	Mice/B6C3F_1
Frequency of Treatment:	Daily
Method:	The 2-year study was part of a larger study involving exposure to boric acid in feed for 14 days, 13 weeks or 2 years. Dietary doses of 0, 0.25 and 0.50% were selected for both sexes of mice in 2-year studies based on body weights and mortality. The effects studied were mortality, clinical signs of toxicity, food consumption, body weight, and histopathology of selected tissues.
GLP:	Yes.
Test Substance:	Boric Acid, 99.7% pure.
Results:	Based on estimates of food consumption, the average amount of boric acid ingested per mouse per day for both sexes was calculated to be 400 to 500 mg/kg in the 0.25% dose group and 1,100 to 1,200 mg/kg in the 0.5% dose group. An increase of mortality of male mice was observed in the high-dose group after week 63 and the 0.25% dose group after week 84. Survival of female mice was not affected at either dose of boric acid. Body weight gain was reduced for males and females in the 0.5% dose group. The most prominent lesion was an increased incidence of testicular atrophy observed in 3/49 (0% dose group), 6/50 (0.25% dose group) and 27/47 (0.5 dose group). There was an increased incidence of interstitial cell hyperplasia in males in the 0.5% dose group (7/47) versus 0/49 (0% dose group) and 0/50 (0.25% dose group). A slight increase in spleen lymphoid depletion in dosed male mice was observed and was considered by the investigators to be due to stress and debilitation. There were marginal increases in subcutaneous tissue tumors and hepatic tumors in dosed male mice; however, these fell within the historical control range and were believed by the investigators to be not related boric acid exposure. The cited tumors are highly variable in historical controls, only occurred in the low-dose group, and were not significant by an incidental tumor test, which is appropriate for tumors that are not a cause of death.
Reference:	NTP (1987) U.S. National Toxicology Program: Toxicology and carcinogenesis studies of boric acid (CAS No. 10043-35-3) in B6C3F1 mice (feed studies). NTP TR 324. DHHS (NIH) Pub. No. 88-2580. NTP, Research Triangle Park, NC (1987).
Reliability:	High because a scientifically defensible or guideline method

was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	Oral – Drinking water
Species/Strain:	Rat/Strain not reported
Frequency of Treatment:	Continuous for 27 weeks
Method:	Male and female rats were continuously fed isopropanol in drinking water for 27 weeks. The dose was 0, 600 or 2,300 mg/kg for males and 0, 1,000 mg/kg or 3,900 mg/kg for females. Exposure groups were compared to controls. The Lowest Observed Effect Level (LOEL) and No Observed Effect Level (NOEL) were determined.
GLP:	No
Test Substance:	2-propanol, purity not reported
Results:	LOEL = 2,300 – 3,900 mg/kg b. w. d. NOEL was 600 – 1,000 mg/kg b. w. d. The male rats showed some decreased body weight gains during the first thirteen weeks of the study, and then increased body weight gain for the remainder of the study. The female rats showed decreased body weight gain throughout the study. No gross or microscopic abnormalities were noted.
Reference:	OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.
Reliability:	Not assignable because limited study information was available.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	Oral – Drinking water
Species/Strain:	Rat/Strain not reported
Frequency of Treatment:	Continuous for 12 weeks
Method:	Male rats were continuously fed isopropanol in drinking water for 12 weeks. The dose was 0, 1, 2, 3 or 5 percent isopropanol in the drinking water solution. Exposure groups were compared to controls. Different physiological endpoints were studied. The LOEL and NOEL were determined.
GLP:	No Data
Test Substance:	2-propanol, purity not reported
Results:	The relative organ weights of liver, kidneys, and adrenals

	were significantly increased in a dose-dependent manner. No histological alterations could be attributed to the dosing, apart from the dose-dependent increase in formation of hyaline casts and droplets in the proximal tubules of the kidneys. Dorsal hippocampal glial fibrillary acidic protein (GFAP) was unaffected after treatment. The NOEL was 1% (870 mg/kg/day) and the LOEL was 2% (1280 mg/kg/day).
Reference:	OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.
Reliability:	Not assignable because limited study information was available.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	Oral – Drinking water
Species/Strain:	Rat/Strain not reported
Frequency of Treatment:	Continuous for 27 weeks
Method:	Male and female rats were continuously fed isopropanol in drinking water for 27 weeks. Five rats per sex per dose and control groups. The dose was 0, 571 mg/kg b. w. d. (0.5% solution) or 2,355 mg/kg b. w. d. (2.5% solution) or a 10% solution for males. The dose was 0, 1,047 mg/kg b. w. d. (1.0% solution) or 3,925 mg/kg b. w. d. (5% solution) for females. Exposure groups were compared to controls. Different physiological endpoints were studied.
GLP:	No
Test Substance:	2-propanol, 99% pure (0.5 – 10% solution in water)
Results:	Mortality: Male 571 mg/kg group (2 of 5); 2,355 mg/kg group (3 of 5); 10% group (5 of 5, results discarded). Female (no mortality observed). Food intake being equal to or greater than that of the control animals, tendency for a decreased fluid intake as 2-propanol concentrations increased (is to be attributed partially to the unpalatable nature and partially to the depressant action of 2-propanol). Retardation of growth and body weight loss of the surviving males in the 571 and 2,355 mg/kg groups (about 5 and 17%, respectively) observed during the first thirteen weeks. A definite body weight gain was noted in the last 14 weeks (5.6% greater in the 571 mg/kg group and 9.1% greater in the 2,355 mg/kg group than those of the control at the end of the 27 weeks. In females, some depression in growth and body weight was noted, which at the termination of the experiment amounted to a 12% loss in the 1,047 mg/kg group and a 10.3% loss in the 3,925 mg/kg

group.

Gross microscopic examination showed no evidence of gross pathologic changes (8 organs examined - not identified).

Reference: Shell Nederland Chemie B.V. Hoogvliet-Rotterdam; Shell, Rotterdam; Industrias Quimicas Asociadas, S.A., Madrid (1944). Published Report (cited in IUCLID (2000). IUCLID DataSet, “Propan-2-ol” (19 February)).

Reliability: Not assignable because limited study information was available.

5.3 Developmental Toxicity

No data for triisopropylborate exists, since the chemical rapidly hydrolyzes to boric acid and isopropanol. Therefore, for this robust summary, supporting data for the hydrolysis products are presented.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type:	Other
Species/Strain:	Rat/Sprague-Dawley (timed-pregnant), Mouse/Swiss (timed-pregnant)
Route of Administration:	Oral – Feed
Exposure Period:	Female: Throughout gestation for 0, 0.1, 0.2, and 0.4% dose groups in both rats and mice. Day 6 to Day 17 of gestation for rats in 0.8% dose group.
Frequency of Treatment:	Continuous
Method:	Female, timed-pregnant Sprague-Dawley rats or Swiss mice (n=26 to 28 per group) were administered boric acid orally via feed throughout gestation. The dose was 0, 0.1, 0.2 or 0.4% boric acid in feed and equated to 0, 78, 163, or 330 mg/kg/day in rats or 0, 248, 452, or 1003 mg/kg/day in mice. An additional group of rats was administered boric acid orally via feed on Days 6 through 15 of gestation. The additional group of rats received a 0.8% dose, which equated to an average dose of 539 mg/kg/day. On Day 17 of gestation for mice, and Day 20 of gestation for rats, the fetuses were weighed and examined for malformations (visceral, skeletal, and external). The exposure groups were compared to the control groups. Maternal and developmental toxicity NOAELs were determined.
GLP:	Not determined
Test Substance:	Boric acid, purity not reported
Results:	<u>Parental Effects</u>: Mouse: Mouse dams exhibited mild renal lesions (≥0.1% dose) and an increase in relative kidney weight (0.4% dose). During treatment increased water intake and decreased weight gain (0.4% dose) was observed. The NOAEL for maternal toxicity in mice approached the low dose of 248 mg/kg (0.1%), with mild renal lesions appearing in only 2 of 10 females. Rat: Maternal rats exhibited increased liver and kidney weights (0.2% dose). Altered water and/or food intake (>0.2% dose), and decreased weight gain (>0.4% dose) was observed during treatment. In rats, the NOAEL for maternal toxicity was 78 mg/kg (0.1%).

Fetal Effects: Mouse: There was a reduction of fetal body weight (≥0.2% dose). An increased incidence of resorptions and malformed fetuses per litter (0.4% dose) was noted. Morphological changes included an increased incidence of short rib XIII and a decreased incidence of rudimentary or full rib(s) at lumbar I, which was construed to be an anatomical variation. The NOAEL for developmental toxicity in mice was 248mg/kg (0.1%).

Rat: Average fetal body weight/litter was reduced at all doses. Prenatal mortality was increased only at the 0.8% dose level. The incidence of fetal malformations was significantly increased at ≥0.2%. The most frequently observed malformations were enlarged lateral ventricles of the brain and shortening of rib XIII. Embryo/fetal toxicity occurred in all groups of rats and the NOAEL was determined to be ≥78 mg/kg (≥0.1%).

Reference: Heindel J.J;, Price C.J., Field E.A, Marr M.C., Myers C.B., Morissey R.F. and Schwetz B.A. *Developmental Toxicity of Boric Acid in Mice and Rats*. Environ Health Perspect (1994), 102 (Suppl. 7), pp.93-97.

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: Other

Species/Strain: Rat/Sprague-Dawley, Mouse/Swiss (CD-1), Rabbit/New Zealand

Route of Administration: Oral – Feed (Rat or Mouse) or Gavage (Rabbit)

Exposure Period: Female: Throughout gestation for 0, 0.1, 0.2, and 0.4% dose groups in both rats and mice. Day 6 to Day 17 of gestation for rats in 0.8% dose group.

Frequency of Treatment: Continuous (mice or rats) or Daily (rabbits)

Method: Female, timed-pregnant Sprague-Dawley rats or Swiss (CD-1) mice (n=26 to 28 per group) were administered boric acid orally via feed from Day 0 to Day 20 or 17 of gestation. The dose was 0, 0.1, 0.2 or 0.4% boric acid in feed and equated to 0, 78, 163, or 330 mg/kg/day in rats or 0, 248, 452, or 1003 mg/kg/day in mice. An additional group of rats was administered 0.8 % (539 mg/kg/day) boric acid orally via feed on Days 6 through 15 of gestation.

Rabbits were artificially inseminated and received 0, 62.5, 125 or 250 mg/kg) boric acid in distilled water via gavage on Days 6 through 19 of gestation.

Maternal body weight, food consumption, water consumption and signs of toxicity were monitored. On Day 17 of gestation for mice, Day 20 of gestation for rats, and Day 30 of gestation for rabbits the uterus was examined and the number of resorptions and dead or live fetuses were determined. Fetuses were weighed. Live fetuses were examined for malformations (visceral, skeletal, and external). The exposure groups were compared to the control groups. Developmental toxicity LOAELs and NOAELs for boric acid were determined for the three animal types.

GLP: Not determined

Test Substance: Boric acid, purity not reported

Results: Parental Effects: Mouse: There were no mortalities. During treatment, increased water intake and decreased weight gain 0.4% (1003 mg/kg/day) was observed in the high dose group. When corrected for uterine weight, the reduction was not significant. The main maternal effect of boric acid was renal pathology. Mild renal lesions for dose groups 0.1% or higher (≥248 mg/kg/day) and an increase in relative kidney weight (1003 mg/kg/day) was observed.

Rat: There were no mortalities. Increased liver and kidney weights at the 0.2% (163 mg/kg/day) dose were observed. Altered water and/or food intake ≥0.2% (≥163 mg/kg/day), and decreased weight gain (>330 mg/kg/day) was observed during treatment.

Rabbit: There were no mortalities. Relative food consumption decreased during treatment (Days 6 – 19) for the 250 mg/kg/day dose group. Relative food consumption increased in the 125 to 250 mg/kg/day dose groups post treatment during days 19 to 30. However, maternal weight gain was significantly reduced in the high dose (250 mg/kg/day) group. Gravid uterine weight was reduced in the mid-dose (125 mg/kg/day) group. When gravid uterine weight was factored with maternal body weight, the reduction in corrected weight for the ≥125 mg/kg/day dose groups was significant ($p \leq 0.05$).

Fetal Effects: Mouse: Prenatal mortality was significantly increased (resorptions = 19% versus 6% in controls) only at the 0.4% (1,003 mg/kg/day) dose level. There was a reduction of fetal male and female body weight in the two highest dose groups (0.2% and 0.4%). The percentage of malformed fetuses per litter was higher than the control group in the 0.4% (1,003 mg/kg/day) dose group. Morphological changes included an increased incidence of short rib XIII, and a decreased incidence of rudimentary or full rib(s) at lumbar I, the latter which was construed to be an anatomical variation. The lowest observed adverse effect level (LOAEL) was determined to be 452 mg/kg/day (0.2%) for fetal weight reduction. The no observed adverse effect level (NOAEL) was 0.2% (452 mg/kg/day).

Rat: Prenatal mortality was significantly increased (resorptions = 36% versus 4% in controls) only at the 0.8% (539 mg/kg/day) dose level. Average fetal body weight/litter was reduced at all doses ranging from 6 to 7% reduction at the 78 mg/kg/day dose to nearly 50% reduction at the 330 mg/kg/day dose. The percentage of malformed fetuses per litter was higher than the control group in the 0.2% (163 mg/kg/day) to the 0.8% (330 mg/kg/day) dose groups. A similar trend in skeletal malformations was observed. The most frequently observed malformations in the 0.4% and 0.8% groups were enlarged lateral ventricles of the brain and shortening of rib XIII. The LOAEL was determined to be 78 mg/kg/day (0.1%) for fetal weight reduction. The NOAEL was <0.1% (78 mg/kg/day).

Rabbit: Prenatal mortality was significantly increased in the high dose (250 mg/kg/day) group only. The percentage of resorptions or fetal deaths per litter (90% of implants per litter versus 6% in controls), the percentage of litters with resorptions or fetal deaths, and the percentage of litters with 100% prenatal mortality (73% versus controls) were increased in this dose group. However, there was no dose related incidence of late fetal deaths as percentages were similar to controls in all exposure groups. The percentage of malformed fetuses per litter were statistically similar to controls in the lowest two exposure groups (62.5 and 125 mg/kg/day) but not the high dose (250 mg/kg/day) group ($p \leq 0.05$). Post hoc analysis of the malformations indicated that 72% in the high dose group were cardiovascular defects versus a 3% incidence rate in controls. Cardiovascular defects included interventricular septal defects (57%) and an enlarged aorta (36%). The LOAEL was determined to be 250 mg/kg/day for prenatal mortality and malformations. The NOAEL was 125 mg/kg/day.

Reference: Heindel J.J, Price C.J. and Schwetz B.A. *The Developmental Toxicity of Boric Acid in Mice, Rats, and Rabbits*. Environ Health Perspect (1994), 102 (Suppl. 7), pp.107-112.

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: Developmental (Benchmark Dose [BMD] study)

Species/Strain: Study A: Rat/Sprague-Dawley (time-mated) – Heindel et al., 1992 (as summarized earlier).

Study B: Rat/Sprague-Dawley (time-mated) – Price et al., 1994-1995 (study not available for summary)

Route of Administration: Oral – Feed

Exposure Period: Female: Day 0 to Day 20 of gestation for 0, 0.1, 0.2, and 0.4% dose groups.

NOTE: Heindel, et al study included exposure to 0.8% boric acid via feed on Day 6 to Day 17 of gestation. This dose group was not included in this BMD study.

Frequency of Treatment: Continuous

Method: Female, timed-pregnant Sprague-Dawley rats (same lot) (n=29/group in Heindel, et al. study and n=60/group in Price study) were administered boric acid orally via feed throughout gestation. In the Heindel study, the dose was 0, 0.1, 0.2 or 0.4% boric acid in feed and equated to 0, 78, 163, or 330 mg boric acid/kg/day. In the Price study, the dose was 0, 0.025, 0.050, 0.075, 0.100 and 0.200% boric acid in feed and equated to 0, 19, 36, 55, 76 and 143 mg boric acid/kg/day. On Day 20 of gestation for rats in the Heindel study, the fetuses were weighed and examined for malformations (visceral, skeletal, and external). On Day 20 of gestation half of the females were sacrificed and the fetuses examined. The fetuses were decapitated prior to examination in the Price study but in the Heindel study fetuses were decapitated after examination. The other mice in the Price study that went to postnatal Day 21 to assess the effects of recovery were not included in the BMD analysis.

Specific endpoints that were significantly related to dose in the Heindel study were selected for analysis. Significance was determined via the application of Mantel-Haenszel trend tests to the dose-response data. Fetal weight and rib-effects were the selected endpoints.

Rib Effects: The relationship of boric acid dose and various rib XIII and lumbar rib effects was analyzed using three different approaches. The first approach involved modeling the dose-related incidence in fetuses with rib XIII effects and modeling the dose-related decrease in fetuses with lumbar ribs by modeling the dose-related increase in fetuses without lumbar ribs. The second approach determined weighted proportions of affected fetuses and third approach calculated rib counts for each fetus by using an algorithm.

Fetal weight effects: The relationship of boric acid dose and fetal weight was analyzed using two approaches. The average live fetal weight for each litter was determined and the averages were considered to be variations of a continuous variable. Second, “adversely low birth weight” was defined as any weight less than the 5th percentile of the fetal weights in the concurrent control group and the number of fetuses per litter that satisfied the definition were counted.

A continuous power model was used to analyze endpoints considered to be on a continuous scale (litter averages for fetal weights, weighted proportions of fetuses with rib effects, and rib counts). In addition to the variance around the mean, separate variances for each dose group were calculated. A log-logistic model was used to assess rib XIII shortening or agenesis, lumbar rib variations, and adversely low birth weight counts.

When defined in terms of benchmark effects (BME), determinations of BMD can yield values close to the NOAEL.

GLP: Not determined

Test Substance: Boric acid (same lot ≤98% purity)

Results: Rib Effects: Because of some data issues and because the benchmark dose for rib effects was greater than fetal weight, the BMD for rib effects was not published.

Fetal weight: The average live fetal weight from the combined data set was used to determine the BMD. The BMD was 59 mg boric acid/kg/day and was close to the NOAEL of 55 mg boric acid/kg/day that was determined in the Price study.

Reference: Allen, B. C.; Strong, P. L.; Price, C. J.; Hubbard, S. A. and Daston, G. P. *Benchmark dose analysis of developmental toxicity in rats exposed to boric acid*. Fund and Appl Tox 32, pp. 194-204 (1996).

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: Other

Species/Strain: Rat/Wistar

Route of Administration: Oral – Drinking water

Exposure Period: Female: Day 6 to Day 16 of gestation.

Frequency of Treatment: Continuous

Method: Female rats were administered isopropanol orally on Days 6 through 16 of gestation. The experiment ended at Day 20 of gestation. The dose was 0, 0.5, 1.25 or 2.5% isopropanol in drinking water. The exposure groups were compared to the control group. Maternal toxicity and teratogenic NOAELs

	were determined.
GLP:	Yes
Test Substance:	2-propanol, purity not reported
Results:	Parental Effects: Body weights significantly decreased starting at Day 7 of gestation and continuing to Day 16 of gestation. Animals in the 1.25% and 2.5% dose groups exhibited reduced food and water consumption during the treatment period. The NOAEL for maternal toxicity was determined to be 0.5% isopropanol. Fetal Effects: In the 1.25% and 2.5% dose groups, fetal body weights were reduced. The reduction was observed for individual fetuses but not for the overall litter. No teratogenic effects were observed. Delayed ossification of the skeleton was observed in the 1.25% and 2.5% dose groups. The finding was attributed to the decrease in maternal body weights during the treatment period. The NOAEL for teratogenicity was determined to be 0.5%.
Reference:	OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.
Reliability:	High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	Teratology
Species/Strain:	Rat/Wistar
Route of Administration:	Oral – Drinking water
Exposure Period:	Female: Day 6 to Day 16 of gestation.
Frequency of Treatment:	Not specified
Method:	Female rats were administered isopropanol orally on Days 6 through 16 of gestation. Sacrifice of females and examination of the maternal reproductive system and fetuses occurred at Day 20 of gestation. The dose was 0, 0.5, 1.25 or 2.5% (596, 1,242, or 1,605 mg/kg/day) isopropanol in drinking water. The exposure groups were compared to the control group. Maternal toxicity and teratogenic NOAELs were determined.
GLP:	Yes
Test Substance:	2-propanol, 99.89% pure
Results:	Parental Effects: All animals in the 1.25% and 2.5% dose groups exhibited reduced food and water consumption during the treatment period. Bodyweights of animals in the

	2.5% dose group were lower than controls from Day 7 of gestation to the end of the study. The NOAEL for maternal toxicity was determined to be 596 mg/kg b. w. isopropanol. Fetal Effects: In the 1.25% and 2.5% dose groups, mean litter weights showed a slight dose-related decrease. In the 1.25% and 2.5% dose groups, mean fetal weights were significantly decreased. No fetal abnormalities were observed. Delayed ossification of the skeleton was observed in the 2.5% dose groups. The finding was attributed to the decrease in mean fetal body weights. The NOAEL for teratogenic effects was determined to be 1,605 mg/kg b. w. isopropanol.
Reference:	Huels, AG (1987). BIBRA submission to US EPA (cited in IUCLID (2000). IUCLID DataSet, "Propan-2-ol" (19 February)).
Reliability:	High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	Teratology
Species/Strain:	Rat/Sprague-Dawley
Route of Administration:	Oral – gavage
Exposure Period:	Female: Day 6 to Day 15 of gestation.
Frequency of Treatment:	Daily
Method:	Time pregnant Sprague-Dawley rats (n=25/group) were administered isopropanol orally on Days 6 through 15 of gestation. The dose was 0, 400, 800 or 1,200 mg/kg/day isopropanol. The dose volume was 5 mL/kg. Maternal body weights and food consumption during gestation were determined every three days. Sacrifice of maternal females occurred at Day 20 of gestation. Maternal body, liver and gravid uterine weights were determined. Ovarian corpora leutea and uterine implants were counted. All live fetuses were weighed, sexed and examined externally. 50% of each litter were examined for visceral and craniofacial abnormalities and the remaining fetuses were examined for skeletal malformations and variations. The exposure groups were compared to the control group. Maternal toxicity and teratogenic NOAELs were determined.
GLP:	Yes
Test Substance:	2-propanol, purity not reported
Results:	Parental Effects: The pregnancy rate was equivalent across all dose groups. No dams aborted, prematurely delivered, or

were removed from the study except for mortality. Two dams of the 1,200 mg/kg b. w. d. dose group died and one dam of the 800 mg/kg b. w. d. dose group died. Gestational weight gain, associated with significantly reduced gravid uterine weight was observed in the 1,200 mg/kg dose group. Otherwise, maternal body weights and weight gain were equivalent. Maternal food consumption was not affected. The NOAEL for maternal toxicity was determined to be 400 mg/kg b. w. isopropanol.

Fetal Effects: Gestational parameters such as pre- and post-implantation loss, fetal sex ratios and litter size were equivalent across dose groups. For the 800 and 1,200 mg/kg dose groups, fetal body weights per litter were significantly reduced. No exposure group had evidence of teratogenic effects. The NOAEL for developmental toxicity was determined to be 400 mg/kg b. w. isopropanol and isopropanol was not considered a CD rat teratogen.

Reference: OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: Teratology

Species/Strain: Rabbit/New Zealand white

Route of Administration: Oral – Gavage

Exposure Period: Female: Day 6 to Day 18 of gestation.

Frequency of Treatment: Daily

Method: Artificially inseminated New Zealand white rabbits were administered isopropanol orally by gavage on Days 6 through 18 of gestation. The dose was 0, 120, 240 or 480 mg/kg/day isopropanol. The dose volume was 2 mL/kg. Maternal body weights and food consumption during gestation were determined every three to six days. Sacrifice of maternal females occurred at Day 30 of gestation. Maternal body, liver and gravid uterine weights were determined. Ovarian corpora leutea and uterine implants were counted.

All live fetuses were weighed, sexed and examined for external, visceral and skeletal malformations and variations. The exposure groups were compared to the control group. The NOAELs for and maternal toxicity and teratogenic effects were determined.

GLP: Yes

Test Substance: 2-propanol, purity not reported

Results: Parental Effects: The pregnancy rate was equivalent across all dose groups. No does aborted, prematurely delivered, or were removed from the study except for mortality. Four does (26.7%) of the 480 mg/kg b. w. d. dose group died. Maternal body weight during treatment was significantly reduced but gestational weight change was not significant for the 480 mg/kg dose group. The 480 mg/kg dose group rabbits showed signs of toxic effects and reduced food consumption. The NOAEL for maternal toxicity was determined to be 240 mg/kg b. w. isopropanol.

Fetal Effects: Gestational parameters such as pre- and post-implantation loss, fetal sex ratios and litter size or fetal body weight per litter were equivalent across dose groups. No exposure group had evidence of teratogenic effects. The NOAEL for teratogenic effects was determined to be 480 mg/kg b. w. isopropanol and isopropanol was not considered a CD rat teratogen.

Reference: OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: Developmental Neurotoxicity

Species/Strain: Rat/CD Sprague-Dawley

Route of Administration: Oral – Gavage

Exposure Period: Female: Day 6 of gestation to Day 21 postpartum.

Frequency of Treatment: Daily

Method: Timed pregnant females (64 sperm positive females per dose group) were administered isopropanol orally on Days 6 of gestation to day 21 postpartum. The experiment ended on Day 68 postpartum. The dose was 0, 200, 700 or 1,200 mg/kg/day isopropanol. The exposure groups were compared to the control group. Maternal toxicity and teratogenic NOAELs were determined.

P1 Females: On Day 68 postpartum the females were evaluated for body, liver and kidney weights and for the number of uterine transplants.

	F1 Males and Females: On Day 0 and 4 pups were counted, examined, weighed and sexed. Litters with insufficient numbers (not specified) of pups were removed from the study. Remaining pups were examined and weighed on Days 7, 13l 17, 21, 36, 49 and 68 postpartum. One male and one female from each litter were selected and assigned to each of three behavioral tests and sacrificed either on Day 2 or Day 68 postpartum. On Day 22 and 68 postpartum, one male and female pup from each litter were weighed and sacrificed. A total of 24 pups were perfused in-situ during the two sacrifices and the CNS and PNS examined.
GLP:	Yes
Test Substance:	2-propanol, >99.95% pure
Results:	Parental Effects: There was one death in the high dose group on Day 15 postpartum. No other substance-related effects were observed. The NOAEL for maternal toxicity was determined to be 700 mg/kg b. w. isopropanol. Fetal Effects: The NOAEL for teratogenic effects was determined to be greater than 1,200 mg/kg b. w. isopropanol. No developmental neurotoxic effects were observed.
Reference:	OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.
Reliability:	High because a scientifically defensible or guideline method was used.

5.4 Reproductive Toxicity

No data for triisopropylborate exists, since the chemical rapidly hydrolyzes to boric acid and isopropanol. Therefore, for this robust summary, supporting data for the hydrolysis products are presented.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type:	Oral – Not specified
Species/Strain:	Rat/Crj:Wistar
Frequency of Treatment:	Daily
Method:	Male Wistar rats six weeks old were given boric acid orally for 4 weeks. Male Wistar rats eight weeks old were given boric acid orally for 2 weeks. The dose was 0, 125, 250 or 500 mg/kg. Exposure groups were compared to controls. All rats were sacrificed at 10 weeks of age. The intent of the study was to assess the validity and limitations of 2-week repeated daily dosing as a means to detect toxic effects to male rodent reproductive organs. At necropsy, the testes and epididymides were weighed and histopathologic specimens prepared using H&E (hematoxylin and eosin) or PAS-H (periodic acid-Schiff reaction and hematoxylin) staining.
GLP:	Not determined
Test Substance:	Boric Acid, purity not reported
Results:	Gross behavior of the rats across all boric acid dose groups in the two or four week studies was not affected. Testicular weights across all boric acid dose groups in the two and four week studies were not affected. Note: Rat spermatids undergo 19 developmental phases and rats have a 12-stage spermatogenesis cycle lasting about 33 days. Spermeation occurs at Stage VIII. <u>Two-week study</u>: Sperm number and motility rate were not decreased in any two or 4-week study groups after 2 weeks of exposure. Histopathologically, retention of step 19 spermatids during stages IX-XI was observed in the testes of almost all rats treated with 500 mg/kg after 2 weeks and indicates a delay in the spermatogenesis cycle. On stage analysis of germinal cells in 2 weeks, spermatogonia and spermatids of stage VII were found to be decreased, and pachytene spermatocytes of stage X were increased indicating spermatid development was delayed and at the third stage of stage 1 of meiosis. Degenerative/necrotic germ cells and multinucleated giant cell formation were observed within 2 weeks, though to a lesser extent following exposure for 4 weeks.

Four-week study: Sperm number and mortality rate decreased in the 250 and 500 mg/kg boric acid dose groups after 4 weeks. Retention of step 19 spermatids during stages IX-XI was observed in the testes of almost all rats treated with 500 mg/kg after 4 weeks indicating a delay in the spermatogenesis cycle.

Reference: Fukuda R, Hirode M, Mori I, Chatani F, Morishima H, Mayahara H. "Collaborative work to evaluate toxicity on male reproductive organs by repeated dose studies in rats 23). A comparative 2- and 4-week repeated oral dose testicular toxicity study of boric acid in rats." J. Toxicol. Sci., October 25, 2000, pp: 223-232.

Reliability: Not assignable because limited study information was available.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: Oral – Gavage

Species/Strain: Rat/Jcl:Wistar

Frequency of Treatment: Daily

Method: Male Wistar rats were given boric acid orally by gavage for 2 or 4 weeks. The dose was 0, 300 or 500 mg/kg. Exposure groups were compared to controls. The two treatment schedules were also compared. The intent of the study was to determine whether a 2-week administration study could evaluate male reproductive toxicity.

GLP: Not determined

Test Substance: Boric Acid, purity not reported

Results: Note: Rat spermatids undergo 19 developmental phases and rats have a 12-stage spermatogenesis cycle lasting about 33 days. Spermeation occurs at Stage VIII.

Two-week study: Decreased testes weights were observed in the high dose (500 mg/kg) group. For both the 300 and 500 mg/kg dose groups, exfoliation of round spermatids, and increased numbers of residual body-like structures in the seminiferous tubules and cell debris in the cranial epididymal ducts were observed histopathologically. Retention of step 19 spermatids was also observed for the top two dose groups. For the 500 mg/kg dose group other histopathologic findings included distorted cytoplasmic lobes of step 19 spermatids, debris in the seminiferous tubules and focal atrophy of the seminiferous tubules with multinucleated giant cell formation and necrotic spermatocytes.

Four-week study: Decreased testis and epididymis weights were observed in the 300 and 500 mg/kg groups.

Histopathological changes in the 300 mg/kg group were similar to those found in the 2-week, 300 and 500 mg/kg groups. Diffuse atrophy of the seminiferous tubules was observed in the 500 mg/kg group.

Reference: Kudo S, Tanase H, Yamasaki M, Nakao M, Miyata Y, Tsuru K, Imai S. *Collaborative work to evaluate toxicity on male reproductive organs by repeated dose studies in rats 24). A comparative 2- and 4-week repeated oral dose testicular toxicity study of boric acid in rats.*" J. Toxicol. Sci., October 25, 2000, pp: 233-239.

Reliability: Not assignable because limited study information was available.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: Two Generation Study (RACB)

Species/Strain: Mice/CD-1 Swiss

Route of Administration: Oral – Feed

Exposure Period: Not available

Frequency of Treatment: Continuous

Method: The method was described as a Reproductive Assessment by Continuous Breeding (RACB). Male and female Swiss CD-1 mice (11 weeks of age at start) were fed boric acid in a powdered diet. Boric acid levels were 1,000, 4,500, and 9,000 ppm. One week later, animals were cohabited for 14 weeks. Pups were evaluated as the litters were born and sacrificed. The last litter was not sacrificed and was weaned and separation of the male parents from the female parents and pups occurred after the delivery. F0 animals from the middle-dose group were mated with controls. After the delivery of the resulting litters, the F0 mice were necropsied. The F1 mice were reared to sexual maturity and consumed the same diet (i.e., boric acid dose) administered to their parents. These animals were mated to non-siblings that had been similarly dosed. The resulting litter was evaluated as before and the F1 mice sacrificed and necropsied.

GLP: Not determined.

Test Substance: Boric acid, purity not reported

Results: F0: Body weight at the end of the study was significantly different ($p \leq 0.05$) in the high (9,000) ppm dose group. Testes weight was significantly different ($p \leq 0.05$) from controls in the middle (4,500 ppm) and high dose groups. The right corpus and head of the epididymis in a significant number of males ($p \leq 0.05$) were different histologically from controls in the middle and high dose groups. Epididymal sperm density in the middle and high dose groups and the percent of epididymal sperm that were mobile in all dose groups were significantly decreased compared to controls.

F1: Mice that received the high dose (9,000 ppm) did not produce any litters. The number of litters per pair was 2.32 ± 0.20 in the 4,500 ppm dose group compared to 4.71 ± 0.12 in the control group. The number of pairs that delivered the first litter was similar to controls but the number of pairs that delivered subsequent litters declined significantly. The difference was significant ($p \leq 0.05$) for this dose group as well as the number of live pups per litter and the adjusted live pup weight (which also decreased from the first litter to subsequent litters).

F1 (4,500 ppm dose group cross-mated with controls): In the group where exposed males were cross-mated to control females, fertility was significantly reduced compared to controls mated to controls. Pup weight was lighter in the group where exposed females were mated to control males versus controls mated to controls. However, the number of pups born/litter was similar.

Reference: Chapin, R. E., and Ku, W. W. The reproductive toxicity of boric acid. Environ Health Perspect, 102 (Suppl 7), pp. 87 – 91 (1994).

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: Male Pathogenesis

Species/Strain: Rat/Strain not reported

Route of Administration: Oral – Feed

Exposure Period: 4, 7, 10, 14, 21 and 28 days

Frequency of Treatment: Continuous

Method: Rat (n=4 for control and total n=6 for treated) were fed boric acid in a powdered diet. The six rats were fed 9,000 ppm for either 4, 7, 10, 14, 21 and 28 days and sacrificed at those time intervals. Treated and control rats were anesthetized and perfused with aldehyde fixative.

Because the testicular lesions caused by boric acid were similar to those caused by androgen insufficiency, a hormone study was also conducted. Additional animals were fed 9,000 ppm boric acid in a powdered diet and sacrificed for testosterone analysis. The time period and number of animals was not specified.

GLP: Not determined.

Test Substance: Boric acid, purity not reported

Results: The first lesion appeared at Day 7 and consisted of an inhibition of sperm release. At Day 21, disorganization of the epithelium and release of immature germ cells was evident. At Day 28, some tubules were atrophic and contained only residual spermatogonia and somatic Sertoli cells. The liver and kidney of the animal dosed for 28 days were sectioned and no abnormalities were noted.

A decrease in circulating testosterone was noted but could not be replicated in subsequent experiments by the authors.

Reference: Chapin, R. E., and Ku, W. W. The reproductive toxicity of boric acid. Environ Health Perspect, 102 (Suppl 7), pp. 87 – 91 (1994).

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: Dose/Time study

Species/Strain: Rat/Strain not reported

Route of Administration: Oral – Feed

Exposure Period: Daily for 9 weeks

Frequency of Treatment: Continuous

Method: Male rats were fed 0, 3,000, 4,500, 6,000 and 9,000 ppm boric acid in feed for 9 weeks for a maximum of 9 weeks. Over the nine week period, 6 rats from each dose group were sacrificed each week and assessed for body and organ weights, sperm parameters, histology of selected organs, clinical chemistries and boron in blood, testis and bone.

Some rats were not sacrificed and after the 9-weeks were fed normal, palletized feed and sacrificed after 8, 16, 24 and 32 weeks (1 through 4 spermatogenesis cycles) post-exposure. Endpoints were similar. Also animals were housed in metabolism cages for 14 days post-exposure and urines collected daily. Blood was collected 1 week and 2 weeks post-exposure.

GLP: Not determined.

Test Substance: Boric acid, purity not reported

Results: Animals consuming 3,000 and 4,500 ppm boric acid had inhibited spermiation but not germ cell death and loss.

Reference: Chapin, R. E., and Ku, W. W. The reproductive toxicity of

	boric acid. Environ Health Perspect, 102 (Suppl 7), pp. 87 – 91 (1994).
Reliability:	High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	One Generation Study
Species/Strain:	Rat/Wistar
Route of Administration:	Oral – Drinking water
Exposure Period:	Female: 21 days prior to mating and thereafter until 21 days post-partum; Male: 70 days prior to mating.
Frequency of Treatment:	Continuous
Method:	Male (n=10 for each exposure group) and Female (n=30 for each exposure group) Wistar rats were administered isopropanol orally via drinking water prior to mating. Males were exposed for a period of 70 days and females were exposed for a period of 21 days prior to mating. The dose was 0, 0.5, 1.0 or 2.0% (0, 456, 835, or 1,205 mg/kg b. w. d for females prior to mating and 0, 1,053, 1,948 or 2,768 mg/kg b. w. d post-partum) isopropanol in the drinking water solution. The dose was 0, 0.5, 1.0 or 2.5% (0, 383, 686 or 1,107 mg/kg b. w. d for males) isopropanol in drinking water prior to mating. Exposure continued for females until the pups were 21 days old. During mating, one male was paired to three similarly exposed females. One of the three females was sacrificed on Day 19 of the pregnancy to determine embryotoxicity. The other two females proceeded to term. Pups were observed for abnormalities and signs of ill health. The pups were weighed on Days 1, 4, 7 and 21. The exposure groups were compared to the control groups. Various parental and neonatal physiological parameters were studied. The Parental and F1 Offspring NOELs were calculated.
GLP:	Yes
Test Substance:	2-propanol, 99.89% pure
Results:	<u>Parental</u>: Rats dosed with 1.0 or 2.0% isopropanol had reduced food and water intakes. Male rats dosed with 2.0% isopropanol had decreased body weights and females given the 1.0 or 2.0% isopropanol had lower body weights in the pre-mating period and during pregnancy. Females given the 2.0% isopropanol were lighter in the post-partum period. The females in the exposed groups and the males exposed to 2.0% isopropanol had lower concentrations of red blood cells. All rats given the 2.0% isopropanol had increased

liver and kidney weights. 97% fertility of the females was observed in the 0.5% exposure group and 80% fertility was observed in females of the control group and other exposure groups. No males were infertile. Fewer pups were born to females exposed to 2.0% isopropanol, but the difference was not significant. The Parental NOEL was determined to be 1.0% for most observations and equated to an average dose of 825 or 625 mg/kg/day for females or males, respectively.

F1 Offspring: By Day 17, survivability of offspring of rats dosed with 2% isopropanol was significantly less than the other groups. The weights of fetuses of the 2.0% exposure group were slightly lower than the controls. 14% of the fetuses in this group had whole body edema. Offspring had a dose-related increase in relative liver weights. No other macroscopic or histopathological changes were noted. A NOEL (increase in relative liver weights) was determined to be 1%.

References: Huels AG, Marl (1988). BIBRA submission to US EPA (cited in IUCLID (2000). IUCLID DataSet, "Propan-2-ol" (19 February)).

Reliability: High because a scientifically defensible or guideline method was used.

Additional Reference for Reproductive Toxicity:

OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: One Generation Study

Species/Strain: Rat/Wistar

Route of Administration: Oral – Drinking water

Exposure Period: Female: 21 days prior to mating and thereafter until pups weaned (3 weeks after birth); Male: 70 days prior to mating.

Frequency of Treatment: Continuous

Method: Male (n-10 for each exposure group) and Female rats (n=10 for each exposure group) were administered isopropanol orally via drinking water prior to mating. Males were exposed for a period of 70 days and females were exposed for a period of 21 days prior to mating. The dose was 0, 0.5, 1.25, 2.0, or 2.5% (0, 517, 1,131, 1,330 or 1,335 mg/kg b. w. d for females prior to mating and 0, 1,167, 2,561, 2,825 or 2,722 mg/kg b. w. d post-partum) isopropanol in the drinking water solution. The dose was 0, 0.5, 1.25, 2.0, or 2.5% (0, 325, 711, 1,002, or 1,176 mg/kg b. w. d for males) isopropanol in drinking water prior to mating. Exposure continued for females until the pups were three weeks old. During mating, one male was paired to a similarly exposed female for 15 days. Pups were observed and weighed at intervals until weaned. The exposure groups were compared to the control groups. Various parental and neonatal physiological parameters were studied. The Parental NOEL was calculated.

GLP: Yes

Test Substance: 2-propanol, purity not reported

Results: Parental: Rats dosed with 1.25, 2.0 or 2.5% isopropanol had reduced food and water intakes starting at Day 1 and had increased liver and kidney weights. Rats dosed with 2.0 and 2.5% isopropanol had decreased body weights from Day 2 to the end of the study. The females in the exposed groups showed signs of anemia. Dams in the 2.5% exposure group showed signs of stress. 100% fertility was observed in all exposure groups. The Parental NOEL was 1.25%.

F1 Offspring: Offspring of rats dosed with 2% or 2.5% isopropanol had unspecified embryotoxic effects.

Reference: Huels AG, Marl (1986). BIBRA Submission to US EPA (cited in IUCLID (2000). IUCLID DataSet, "Propan-2-ol" (19 February)).

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type: Two Generation Study

Species/Strain: Rat/Sprague-Dawley

Route of Administration: Oral – Gavage

Exposure Period: P1 Female: 10 weeks prior to mating and thereafter until weaning of F1 generation; P1 Male: 10 weeks prior to mating. F1/P2 Female: 10 weeks prior to mating and thereafter until weaning of F2 generation; F1/P2 Male: 10 weeks prior to mating.

Frequency of Treatment: Daily

Method: Male and female Sprague-Dawley rats were administered isopropanol orally via gavage prior to mating. Males and females were exposed for a period of 10 weeks prior to mating. The dose was 0, 100, 500 or 1,000 mg/kg b. w. d. Exposure continued for females until the pups were weaned. The F1/P2 generation was similarly exposed and dosing started at Day 21 postpartum.

The exposure groups were compared to the control groups. Various parental and neonatal physiological parameters were studied. The Parental, F1 Offspring and F2 Offspring NOAELs were calculated.

GLP: Yes

Test Substance: 2-propanol, purity not reported.

Results: Parental (P1): Animals dosed with 1,000 mg/kg/day isopropanol had increased had increased absolute and/or relative liver weights. Males dosed with 1,000 mg/kg/day isopropanol had increased absolute and/or relative kidney weights, which was attributed to hyaline droplet neuropathy. Increased absolute or relative liver weights were observed in parental animals dosed with 500 mg/kg/day compared to controls, but these effects were not considered to be an adverse effect. The P1 NOAEL was 500 mg/kg/day.

F1/P2 Offspring: Increased mortality of F1 offspring of P1 rats dosed with 1,000 mg/kg/day was observed. Reduced body weight of F1 offspring of P1 rats dosed with 1,000 mg/kg/day was observed. Some males exposed to 1,000 mg/kg/day isopropanol had centrilobular hepatocyte hypertrophy. No other macroscopic or histopathological changes were noted. No treatment-related postmortem findings were observed. The F1 NOAEL was 500 mg/kg b. w.

F2 Offspring: Reduced body weight of F2 male and female offspring of F1/P2 rats dosed with 1,000 mg/kg/day was observed. No treatment-related postmortem findings were observed. The F2 NOAEL was 500 mg/kg/day. The reproductive NOAEL was greater than 1,000 mg/kg/day.

NOTE: The study-derived NOELs for the F1 and F2 offspring are contingent upon the biological significance ascribed to the effects observed for the 500 mg/kg /day treatment group. There are two perspectives on the interpretation of these observations. A conservative perspective is that the reductions in postnatal survival are treatment- and dose-related effects (U.S. EPA, 1992 U.S. EPA, 1996; Tyl, 1996). Consequently, the NOEL based on this interpretation would be set at 100 mg/kg/day. On the other hand, the NOEL may be set at 500 mg/kg/day if these observations are not deemed biologically significant (Bevan *et al.*, 1995; Harris, 1995). A benchmark dose (BMD) assessment was conducted for the CMA Isopropanol Panel as a way of clarifying issues surrounding the derivation of effect levels for this study. As described below, this assessment resulted in calculated BMD dosages of 449 and 418 mg/kg low/day for the F1 and F2, respectively as appropriate descriptors for this endpoint.

Reference:	OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.
Reliability:	High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	Benchmark Dose Study (BMD)
Species/Strain:	Rat/Sprague-Dawley
Route of Administration:	Oral – Gavage
Exposure Period:	NA
Frequency of Treatment:	NA
Method:	Quantitative Dose-Response Analysis using the benchmark dose method (BMD) to identify the relevant dosage to derive a toxicity value that may contribute in part to safety assessment decisions for isopropanol. The BMD was conducted for the CMA Isopropanol Panel as a way of clarifying issues surrounding the derivation of effect levels for the above two-generation study.
GLP:	No Data
Test Substance:	See above two-generation study.
Results:	Based upon decrease in mating index observed in the P2 males, a BMDL10 of 407 mg/kg/day was estimated for reproductive effects. A BMDL5 of 418 mg/kg/day was estimated for developmental effects based upon the F2 generation 4-day survival. For the F1 generation 4-day survival, 449 mg/kg bw/day was estimated as BMDL5. The corresponding MLE dosages were 786 (Polynomial model) and 771 mg/kg bw/day (Weibell model) for the reproductive effects, 656 mg/kg bw/day for the F1 postnatal effects, and 804 mg/kg bw/day for the F2 postnatal effects.
Reference:	OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.
Reliability:	High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	One Generation Study with Teratologic Observations
Species/Strain:	Rat/Wistar
Route of Administration:	Oral – Drinking water
Exposure Period:	Female: Not specified, Male: Not specified.
Frequency of Treatment:	Continuous
Method:	Male and Female Wistar rats were administered isopropanol orally via drinking water prior to mating. The dose was 3% isopropanol in the drinking water solution. Exposure continued for 10 days and then the females and surviving pups were given water that did not contain isopropanol. Various parental and neonatal physiological parameters were studied. The exposed parental animals were re-exposed to 2% isopropanol and re-mated as in the 3% study to provide litters for this developmental toxicity study. At day 20 of gestation, the dams were cesarean sectioned. Selection of the F1 pups for mating was delayed for 2-weeks. The F1 animals were exposed to 2% isopropanol and mated. After a set of litters had been produced, the F1/P2 generation animals were sacrificed for gross and microscopic evaluation.
GLP:	No
Test Substance:	2-propanol, purity not reported
Results:	3% Dose: Growth was moderately depressed and by the 9th week these animals were slightly smaller than the F1/P2 2% dose group. Fertility (a 73% pregnancy rate) was reduced. At 7 to 10 days postpartum, pup development was slowed significantly and mortality rate was higher than the F1/P2 2% dose group offspring. 2% Dose: (P1 & F1/P2) Pregnancy rates and survival of the females receiving 2% isopropanol were not affected. The body weight of pregnant females was not depressed. However, growth of weanling rats was significantly depressed and in utero fetus weight was also significantly depressed. There was evidence of retarded skeletal maturation of the in utero fetuses and suggests that 2% isopropanol administered orally could be a rat teratogen. The fetotoxicity was considered "minimal" by the researchers because other parameters such as nidation and early or late fetal deaths were not detectably affected. No significant findings as regards the F2 generation produced by the 2% isopropanol dosed F1/P2 rats.

Hematological, biochemical and urinary data obtained terminally on F1/P2 rats were within normal ranges. Changes in kidneys included accelerated appearance of tubular casts and focal tubular regeneration, microcyst development in the apices of renal papillae, and possible epithelial degeneration in tubules in the outer medullar zone. The kidney findings were attributed to diuretic effects induced by the isopropanol.

Reference: OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.

Reliability: Not assignable because limited study information was available.

5.5 Genetic Toxicity

Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strain:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537, and TA1538
Exogenous Metabolic Activation:	With and without rat liver homogenate activation system (S9)
Exposure Concentrations:	0, 1,000, 3,000, 5,000, 7,000, and 10,000 μg/plate
Method:	No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The assay (not a closed system assay) was performed as 2 independent trials with 2 replicates per concentration in the presence and the absence of a rat liver homogenate activation system (S9). In the absence of an activation system, a solution of the test substance and approximately 10^8 bacteria in 0.1 mL were added to top agar. These components were mixed and poured on the surface of a plate containing Davis minimal agar. To treat in the presence of an activation system, S9 mix was added to the bacteria-test sample-top agar mixture. S9 was the 9000 x g supernatant of liver homogenate from rats given Aroclor 1254 5 days before sacrifice. The S9 mix contained S9, $MgCl_2$, KCl, glucose-6-phosphate, NADP, and sodium phosphate (pH 7.4). The S9 mix was added to the bacteria, test sample, and top agar. These components were mixed and immediately poured over the minimal agar plate. The revertant colonies were counted after the plates were incubated at 37°C for 48-hours. Positive controls included 2-aminoanthracene (2AA), N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), 9-aminoacridine (9AAc), and 2-nitrofluorene (2NF). The solvent control was acetone.

The cytotoxicity of the test substance in the presence and absence of an activation system, as measured in strain TA1535, was the basis for selecting concentrations to be used in the mutagenesis experiment. The protocol used to determine the cytotoxicity was identical to the mutagenesis protocol, except that 10^3 rather than 10^8 bacteria were used per plate and a nonlimiting concentration of histidine was present. Concentrations of test sample that were nontoxic and, if possible, slightly toxic were selected for the mutagenesis assay.

Data from replicate plates within a single experiment were averaged. The average of those values from different experiments was determined. The highest average number of revertants that was obtained was expressed as a multiple of the control value for the sensitive strain(s). When a test sample was active, the average numbers of revertants observed before activity plateaus or decreases at the various concentrations tested were submitted to linear regression analysis. The slope of the line thus obtained was used to determine the number of revertants/nmole or µg of test sample.

The test material was classified as nonmutagenic if the reversion frequency was less than 2 times the spontaneous frequency, if less than 0.02 revertants/nmole were observed. No additional statistical analysis was performed.

GLP: No

Test Substance: Triisopropylborate, actual purity not reported (test substance reported as "pure")

Results: Negative

Remarks: The initial cytotoxicity experiment with strain TA1535 failed to demonstrate a toxic effect for the test substance at the concentrations tested. Higher concentrations were not included in the mutagenesis experiments.

The test substance was not mutagenic in the presence or absence of an activation system. Additional details for solvent control, test substance (TIPB), and positive controls can be found in the tables below. A dash (-) indicates no data.

Trial 1 (with metabolic activation)						
Concentration (µg/plate)		Histidine$^+$ revertants per plate (average of 2 plates)				
		TA1535	TA1537	TA1538	TA98	TA100
Acetone		14	6	19	28	148
TIPB	1000	19	5	30	30	144
	3000	25	5	25	29	140
	5000	24	10	24	33	174
	7000	18	6	29	45	151
	10,000	16	8	29	171	217
2AA	5	-	-	-	-	1296
	10	693	-	1736	2251	-
	100	-	543	-	-	-

Trial 1 (without metabolic activation)						
Concentration (µg/plate)		Histidine$^+$ revertants per plate (average of 2 plates)				
		TA1535	TA1537	TA1538	TA98	TA100
Acetone		20	1	16	24	162
TIPB	1000	29	6	13	12	127

	3000	27	8	11	18	137
	5000	22	7	9	15	155
	7000	30	9	10	14	145
	10,000	25	5	12	15	139
MNNG	2	1519	-	-	-	1544
9AAc	50	-	899	-	-	-
2NF	25	-	-	1851	2314	-

Trial 2 (with metabolic activation)						
Concentration (µg/plate)		Histidine+ revertants per plate (average of 2 plates)				
		TA1535	TA1537	TA1538	TA98	TA100
Acetone		18	8	19	24	179
TIPB	1000	17	10	21	30	182
	3000	26	11	19	17	186
	5000	24	8	22	22	182
	7000	34	10	20	21	182
	10,000	23	6	28	17	188
2AA	5	-	-	-	-	1604
	10	524	-	1265	1582	-
	100	-	467	-	-	-

Trial 2 (without metabolic activation)						
Concentration (µg/plate)		Histidine+ revertants per plate (average of 2 plates)				
		TA1535	TA1537	TA1538	TA98	TA100
Acetone		27	8	13	23	148
TIPB	1000	21	6	13	22	138
	3000	31	8	11	22	179
	5000	26	4	16	18	150
	7000	26	6	13	23	171
	10,000	23	8	13	18	169
MNNG	2	2222	-	-	-	2229
9AAc	50	-	653	-	-	-
2NF	25	-	-	2151	2325	-

Trial 3 (without metabolic activation)						
Concentration (µg/plate)		Histidine+ revertants per plate (average of 2 plates)				
		TA1535	TA1537	TA1538	TA98	TA100
Acetone		-	7	-	-	-
TIPB	1000	-	8	-	-	-
	3000	-	8	-	-	-

	5000	-	11	-	-	-
	7000	-	11	-	-	-
	10,000	-	8	-	-	-
9AAc	50	-	1011	-	-	-

Reference: DuPont Co. (1978). Unpublished Data, Haskell Laboratory Report No. 304-78, "Mutagenic Activity in the *Salmonella*/Microsome Assay" (June 9).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for *In vitro* Bacterial Reverse Mutation Assay: None Found.

5.6 *In vitro* Clastogenicity Studies – No Data

5.7 *In vivo* Genetic Toxicity

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type: Micronucleus Assay

Species/Strain: Mice/Swiss Webster

Route of Administration: Oral – Gavage

Exposure Period: Two days, Bone marrow examined 24 and 48 hours after administration.

Frequency of Treatment: Once daily for 2 days.

Method: Study conducted in accordance to EPA FIFRA guidelines (40 CFR 158.340). Male and female Swiss Webster mice administered oral dose of 0, 225, 450, 900, 1,800 or 3,500 mg/kg b. w. d boric acid via gavage on 2 days. Bone marrow examined 24, 48 or 72 hours after last treatment.

GLP: Yes

Test Substance: Boric Acid, purity not reported.

Results: Negative.

Reference: Borax Consolidated LTD, Guilford (1991). SRI International, Study No. 2389-C400-91 (cited in IUCLID (2000). IUCLID Data Set, "10043-35-3" (18 February)).

Reliability: High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Type:	Micronucleus Assay
Species/Strain:	Mice/ICR random bred
Route of Administration:	Intraperitoneal
Exposure Period:	Single dose, Bone marrow examined 24, 48 and 72 hours after administration.
Frequency of Treatment:	Single dose
Method:	Study conducted in accordance to EPA TSCA guidelines (40 CFR 798.5395). Male and female ICR random bred mice administered intraperitoneal dose of 350, 1,173 or 2,500 mg/kg isopropanol. Bone marrow examined 24, 48 or 72 hours after treatment.
GLP:	Yes
Test Substance:	Isopropanol, purity not reported.
Results:	Negative.
Reference:	OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.
Reliability:	High because a scientifically defensible or guideline method was used.

5.8 Carcinogenicity

Data for Hydrolysis Product: Boric Acid (10043-35-3)

Type:	Oral – Feed
Species/Strain:	Mice/B6C3F_1
Frequency of Treatment:	Daily
Method:	The 2-year study was part of a larger study involving exposure to boric acid in feed for 14 days, 13 weeks or 2 years. Dietary doses of 0, 0.25 and 0.50% were selected for both sexes of mice in 2-year studies based on body weights and mortality. The effects studied were mortality, clinical signs of toxicity, food consumption, body weight, and histopathology of selected tissues.
GLP:	Yes.
Test Substance:	Boric Acid, 99.7% pure.
Results:	There were marginal increases in subcutaneous tissue tumors and hepatic tumors in dosed male mice; however, these fell within the historical control range and were believed by the investigators to be not related boric acid exposure. The cited tumors are highly variable in historical controls, only occurred in the low-dose group, and were not significant by an incidental tumor test, which is appropriate for tumors that are not a cause of death.
Reference:	NTP (1987) U.S. National Toxicology Program: Toxicology and carcinogenesis studies of boric acid (CAS No. 10043-35-3) in B6C3F1 mice (feed studies). NTP TR 324. DHHS (NIH) Pub. No. 88-2580. NTP, Research Triangle Park, NC (1987).
Reliability:	High because a scientifically defensible or guideline method was used.

Data for Hydrolysis Product: Isopropanol (67-63-0)

Species/Strain:	Mouse/CD-1
Route of Administration:	Inhalation
Exposure Period:	18 months
Frequency of Treatment:	6 hrs/day, 5 days/week
Method:	Male and Female CD-1 mice were exposed to 0, 500, 2,500 or 5,000 ppm isopropanol via inhalation. Exposure was for 6 hours/day, 5 days/week over an 18 month period. The study protocol followed EPA TSCA test guidelines and included recovery groups for each dose. Mortality, morbidity, behavior and other clinical observations and other

physiological parameters were studied. A NOEL for toxicity and a NOEL for oncogenesis were determined.

GLP: Yes

Test Substance: 2-propanol, purity not reported

Results: 500 ppm Dose: There was no increase in the frequency of neoplastic lesions in this dose group versus controls. No difference in mortality rate and mean survival time from the control group was observed. Absolute and relative liver weights were increased in both sexes. Relative testis weights were decreased. A significant number of females had mild to moderate degrees of tubular dilation. This finding was not duplicated in male mice and smaller numbers of females in the higher dose groups had this finding. There was no evidence of tubular cell degeneration or urinary outflow obstruction. Hematological parameters were not affected. The uncertainty regarding kidney effects lead to a NOEL for toxicity of 500 ppm.

500 ppm Dose (Recovery Group): The recovery group did not have any increased incidence of kidney effects. Nor was there a decrease in testis weights. A concentration related absolute and relative increase in liver weight was observed in males but not females.

2,500 ppm Dose: There was no increase in the frequency of neoplastic lesions in this dose group versus controls. No difference in mortality rate and mean survival time from the control group was observed. Narcosis was observed during exposure. Clinical signs in some males and females included hypoactivity, and lack of a startle reflex. Both sexes had increased body weight and/or body weight gain. Absolute and relative liver weights were increased in both sexes. Relative testis weights were decreased. Microscopic evaluation of the seminal vesicles showed increased incidence of dilation.

2,500 ppm Dose (Recovery Group): Male mice continued to increase in these body weight and/or body weight gain post-exposure. The recovery group did not have any increased incidence of kidney effects. Nor was there a decrease in testis weights. A concentration related absolute and relative increase in liver weight was observed in males but not females. Microscopic evaluation of the seminal vesicles did not indicate any dilation as was observed in the non-recovery males. A NOEL of 2,500 ppm for clinical signs was determined.

5,000 ppm Dose: There was no increase in the frequency of neoplastic lesions in this dose group versus controls. The NOEL was determined to be >5,000 ppm for oncogenetic effects. No difference in mortality rate and mean survival time from the control group was observed. Clinical signs in some males and females included hypoactivity, lack of a startle reflex, ataxia and prostration (males only). Both sexes had increased body weight and/or body weight gain. Absolute and relative liver weights were increased in both sexes. Relative testis weights were decreased. Microscopic evaluation of the seminal vesicles showed increased incidence of dilation.

5,000 ppm Dose (Recovery Group): Male mice continued to increase in these body weight and/or body weight gain post-exposure. The recovery group did not have any increased incidence of kidney effects. Nor was there a decrease in testis weights. A concentration related absolute and relative increase in liver weight was observed in males but not females. Microscopic evaluation of the seminal vesicles did not indicate any dilation as was observed in the non-recovery males.

Reference: OECD (1997). 2-Propanol CAS #67-63-0 Screening Information Data Set (SIDS) Initial Assessment Report (SIAR). Organization for Economic Co-operation and Development (OECD). March 1997.

Reliability: High because a scientifically defensible or guideline method was used.